

THE ENDOCRINOLOGIST

THE MAGAZINE OF THE SOCIETY FOR ENDOCRINOLOGY

Exercise

IT'S GOOD TO MOVE IT, MOVE IT

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A word from THE EDITOR...



Welcome to *The Endocrinologist* in 2020! New year, new Editor – I hope you find the next eight issues both thought-provoking and entertaining. I thank Amir for doing a great job for the last 2 years.

As well as a new Editor, your Society has a new President. On page 24, Raj Thakker sets out his vision for the Society for Endocrinology.

It's an Olympic year, so we thought we would 'kick off' with exercise, looking at the variety of benefits we gain from keeping active. David Dearlove and colleagues describe the metabolic benefits of exercise on page 7. Meanwhile, on page 14, Sarah Leyland and Jon Tobias talk us through the Royal Osteoporosis Society's recent 'Strong, Steady and Straight' exercise recommendations, which are designed to improve bone health in osteoporosis. Exercise is important across the life course: Katy Kuhrt and Andrew Shennan discuss exercise during pregnancy (page 19) and Lawrence Hayes describes the benefits of exercise when ageing (page 12).

March 8 was International Women's Day. To mark this, Anne White, 2020 recipient of the Society for Endocrinology's Jubilee Medal, tells us about her career and rounded approach to leadership on page 31. She highlights the importance of encouraging women to speak up about their work. This theme is also taken up by Victoria Salem and colleagues on page 30, who found that only 21% of questions at SfE BES 2017 were asked by women, but that more women asked questions if there was a female Chair. We are still a way off equality and diversity, in spite of gender balance for attendance at the annual Society for Endocrinology BES conference.

Compared with Olympic athletes and other sporting heroes, we mere mortals may only dream of sporting greatness. However, this issue will hopefully inspire you to keep up any exercise-related New Year resolutions that you made, as well as providing you with useful information to support discussions with your patients. Who knows, it may assist you in achieving your own sporting glory!

Best wishes

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Become a contributor... Contact the Editorial office at **endocrinologist@endocrinology.org**

The Society welcomes news items, contributions, article suggestions and letters to the Editor. We would also like to hear your feedback on this issue of the magazine.

Deadline for news items for the Summer 2020 issue: **3 April 2020.**

Front cover image ©Shutterstock

CHANGES AT THE ENDOCRINOLOGIST

Thank you, Amir Sam, for all your great work on this magazine! Amir's term as Editor finished at the end of 2019. Please join us in welcoming Helen Simpson as our new Editor and Kim Jonas as Associate Editor.

Any Society member who is interested in contributing to *The Endocrinologist*, either as an author or as a member of the Editorial Board, should email media@endocrinology.org for more details.



Helen Simpson



Kim Jonas

REACH THE WIDER ENDOCRINE COMMUNITY AT SFE BES 2020

Apply for our Early Career Prize Lectures for the chance to present your work at the Society for Endocrinology BES conference 2020 in Harrogate. Successful applicants also receive a £750 honorarium and publish an article on their work in *The Endocrinologist*. You must submit your abstract by 18 May. See www.endocrinology.org/grants-and-awards/prizes-and-awards/early-career-prize-lectures.



INSPIRE THE NEXT GENERATION

With a Society Summer Studentship, you could fund an undergraduate student to gain experience in your lab this summer. The application deadline is 18 March.

Find out more at www.endocrinology.org/grants-and-awards/grants/summer-studentships.

NEW FOR 2020! MEETINGS SUPPORT GRANTS

Keep an eye open for the launch of our new Meetings Support Grants this spring. We have simplified and streamlined our funding opportunities to help you organise a wider variety of Society-endorsed events. More details will be coming your way soon. The application deadline will be Wednesday 27 May.

NEW GUIDELINES FOR THE PERI-OPERATIVE MANAGEMENT OF ADRENAL INSUFFICIENCY

The Society for Endocrinology, the Association of Anaesthetists and the Royal College of Physicians have published, *Guidelines for the management of glucocorticoids during the peri-operative period for patients with adrenal insufficiency* in the journal *Anaesthesia* (doi.org/10.1111/anae.14963).

SUMMARY OF NICE GUIDANCE ON TREATING THYROID DISEASE

The *BMJ* have published a summary of some of the most recent recommendations from the NICE guideline *Thyroid disease: assessment and management* (doi.org/10.1136/bmj.m41).

ADVERTISE YOUR JOBS TO OVER 3,000 ENDOCRINOLOGISTS

Post your vacancies directly on SFE Connect to quickly and easily share with our endocrine community, or email them to media@endocrinology.org. Not yet a member of SFE Connect? Visit www.endocrinology.org/join-sfe-connect to join the conversation.

SUPPORT TO FURTHER YOUR CAREER

Don't miss these approaching deadlines for Society grants, which are available to help fund your research, travel or lab equipment:

- a **Practical Skills Grant** will help you forge new collaborations or learn skills by funding a visit to another institution or attendance at a workshop: apply by **8 April**.
- the Society's **Early Career Grants** provide financial support to boost your research: apply by **6 May**.
- an **Equipment Grant** could buy vital equipment for your laboratory: apply by **6 May**.
- **Endocrine Nurse Grants** help fund projects that enhance nursing clinical practice: apply by **6 May**.

Visit www.endocrinology.org/grants-and-awards for full details of how to apply, and for more Society funding opportunities.

REGISTER FOR OUR WORKSHOP ON THE USE OF RADIOIODINE FOR THYROID DISEASE

Join us for our one-day workshop on the use of radioiodine in benign thyroid disease in Birmingham on 24 April. This established course represents an essential component of the new national training scheme for ARSAC certification for iodine-131 administration in the treatment of benign thyroid disease.

SOCIETY CALENDAR

ENDOCRINE ACADEMY:

20 & 21 April 2020
CLINICAL UPDATE 2020
Birmingham, UK

20 April 2020
CAREER DEVELOPMENT WORKSHOP 2020
Birmingham, UK

24 April 2020
NATIONAL TRAINING SCHEME FOR THE USE OF RADIOIODINE IN BENIGN THYROID DISEASE
London, UK

16-18 November 2020
SFE BES 2020
Harrogate, UK

www.endocrinology.org/events
for full details

SOCIETY ENDORSED EVENTS

4 September 2020
EUROPEAN YOUNG ENDOCRINOLOGY SOCIETY (EYES) CONFERENCE 2020
Birmingham, UK

24 November 2020
OXFORD ENDOCRINE MASTERCLASS 2020
Oxford, UK

SOCIETY SUPPORTED EVENTS

25 March 2020
14th ANNUAL INTERNATIONAL WORKSHOP ON RESISTANCE TO THYROID HORMONE AND THYROID HORMONE ACTION
Monterey, CA, USA

2 July 2020
GUT-BONE AXIS MEETING
Norwich, UK

GRANT AND PRIZE DEADLINES

18 March 2020
PATIENT SUPPORT GRANTS

18 March 2020
SUMMER STUDENTSHIPS

25 March 2020
PUBLIC ENGAGEMENT GRANTS

8 April 2020
PRACTICAL SKILLS GRANTS

30 April 2020
UNDERGRADUATE VIDEO PRIZE

6 May 2020
EARLY CAREER GRANTS

6 May 2020
ENDOCRINE NURSE GRANTS

6 May 2020
EQUIPMENT GRANTS

13 May 2020
LEADERSHIP & DEVELOPMENT AWARDS PROGRAMME

18 May 2020
EARLY CAREER PRIZE LECTURES

www.endocrinology.org/grants
for full details of all Society grants and prizes

SOCIETY FOR ENDOCRINOLOGY OFFICIAL JOURNALS

Society members have free access to the current content of *Journal of Endocrinology*, *Journal of Molecular Endocrinology*, *Endocrine-Related Cancer* and *Clinical Endocrinology* via the members' area on the Society home page, www.endocrinology.org. *Endocrine Connections* and *Endocrinology, Diabetes & Metabolism Case Reports*, the Society-endorsed case reports publication, are open access and free to all.



JOURNAL OF ENDOCRINOLOGY

EDITOR'S CHOICE

Glucocorticoid and mineralocorticoid receptors in postnatal growth

Glucocorticoids work with the immune system to treat a wide range of health problems. Their use, however, is associated with a number of side effects, including growth retardation and skeletal frailty. The mechanisms by which they induce growth retardation are unclear. This study determined whether the observed growth retardation was dependent on activation of both the glucocorticoid receptor (GR) and the mineralocorticoid receptor (MR).

Faught & Vijayan studied ubiquitous GR- or MR-knockout zebrafish with or with hydrocortisone

during early postnatal life. In the absence of GR, hydrocortisone exposure led to protein accumulation, indicating that MR activation led to an anabolic response. Conversely, hydrocortisone-mediated reduction in body mass and protein content required activation of both GR and MR, as activation of GR alone did not lead to reduced protein content.

This is the first study to show that activation of both GR and MR is required for glucocorticoid-induced growth suppression during postnatal development.

Read the full article in *Journal of Endocrinology* **244** 261–271



Colin Farquharson

JOURNAL OF MOLECULAR ENDOCRINOLOGY

EDITOR'S CHOICE

GLP-1 receptor activation and cancer cell chemosensitivity

Glucagon-like peptide-1 (GLP-1) receptor agonists are now widely used for the treatment of type 2 diabetes and obesity. Some of these compounds, including liraglutide, also decrease cardiovascular morbidity and mortality in patients with type 2 diabetes. However, some initial experimental studies on rodent models have raised concerns that GLP-1 receptor activation by these agonists may increase the risk of pancreatitis and pancreatic cancer. Large scale clinical trials have not confirmed these concerns in humans.

Zhao *et al.* aimed to determine whether and how the GLP-1 receptor agonist liraglutide affects the chemoresistance and chemosensitivity of pancreatic

cancer cells to gemcitabine *in vitro* and *in vivo*. They showed that addition of liraglutide does not increase cancer cell growth but rather the opposite – incubation with liraglutide dose-dependently inhibited the growth and promoted the apoptosis of several pancreatic cancer cell lines.

While these data certainly cannot be extrapolated to humans, they provide another important piece of scientific evidence suggesting that GLP-1 receptor agonist-based therapies are safe and can be used in the wide population of patients with obesity and type 2 diabetes.

Read the full article in *Journal of Molecular Endocrinology* **64** 103–113



Martin Haluzik

ENDOCRINE-RELATED CANCER

Soluble CD105 is prognostic of prostate cancer recurrence

Prostate cancer is the most common cancer in men. Although the 5-year survival rate is near 100%, up to 35% of patients will develop recurrent disease. High risk patients are increasingly undergoing radical prostatectomy, which is curative in many cases. Additional therapies have substantial comorbidities and are not warranted, unless there is a high probability of disease recurrence. A reliable prognostic biomarker to identify patient recurrence status at the time of surgical intervention is needed, to support management of adjuvant therapy.

Soluble endoglin (sCD105) is a cell surface transforming growth factor- β co-receptor that has been described as a serum biomarker in breast, colon and prostate cancer. Placencio-Hickok *et al.* examined sCD105 as a blood-based

prognostic biomarker for disease recurrence following prostatectomy. They assessed plasma samples from 181 prostate cancer patients which had been collected in 2002–2012 from prostatectomy cases from the Prostate Cancer Biorepository Network at the University of Washington.

Elevated sCD105 was found to be associated with recurrence-free survival of prostate cancer patients. There was an inverse correlation of presurgical prostate-specific antigen and sCD105 within 5 years of prostatectomy. There was no significant association of sCD105 with either Gleason grade or pathologic stage of the disease. Thus, sCD105 may serve as a prognostic biomarker to determine prostate cancer recurrence, which may aid in treatment decision-making following radical prostatectomy.

Read the full article in *Endocrine-Related Cancer* **27** 1–9

CLINICAL ENDOCRINOLOGY

Evolution of macroprolactinomas during pregnancy

Management of any endocrine disorder during pregnancy brings additional challenges, as there is the safety of two people to consider, as well as the impact of the endocrine conditions on the disease process. Barraud and colleagues have described 85 pregnancies in women with macroprolactinoma, in a multicentre, retrospective study which provides useful information.

Adenoma size was >20mm in 30.4% of the patients. Progression was defined by relevant clinical symptoms. Patients were followed clinically with visual field assessment. Twelve cases of tumour growth occurred (14.1%) in nine patients (19.6%); three of these had clinically significant tumour

growth and two required surgery during pregnancy due to tumour growth threatening vision. Dopamine receptor agonist (DA) was discontinued in 64% had, with the remainder continuing on DA. No pre-pregnancy features predicted increase in size of the macroprolactinoma during pregnancy.

There is no accepted clinical guidance, and whilst the literature says to discontinue DA during pregnancy, there is the view that DA should be continued for macroprolactinoma. The current paper adds to our knowledge of macroprolactinoma during pregnancy and reminds us that careful observation is needed to pick up those patients whose tumours are enlarging.

Read the full article in *Clinical Endocrinology*
<https://doi.org/10.1111/cen.14162>

ENDOCRINOLOGY, DIABETES & METABOLISM CASE REPORTS

Cardiac disease complicating Graves' disease in young adults

The care of young adults with hyperthyroidism constitutes a reasonable portion of clinical endocrine outpatient work. Here, Witczak and colleagues remind us of the risk of cardiac complications from uncontrolled thyroid overactivity. The myocardium, vasculature and autonomic nervous system are all directly affected by thyroid hormones. Tachyarrhythmias and cardiomyopathy, eventually resulting in cardiac decompensation, can result from thyroid hormone excess.

The authors report the cases of three patients, aged 28, 34 and 42, who developed significant cardiac disease having had symptoms

suggestive of thyrotoxicosis for weeks to months. None of the patients had prior history of heart problems, yet all presented with cardiomegaly with or without pericardial effusion with or without reduced ejection fraction.

All three were treated supportively and underwent early definitive treatment for their Graves' disease. Importantly, considerable improvements in cardiac health were observed for each patient, following treatment of the thyroid overactivity.

Read the full article in *Endocrinology, Diabetes & Metabolism Case Reports*
EDM190132

ENDOCRINE CONNECTIONS

Long term efficacy of metformin in overweight-obese PCOS

Metformin is widely used in the treatment of women with polycystic ovary syndrome (PCOS), yet data supporting its long term efficacy in this population are scant.

In this retrospective cohort study, Jensterle *et al.* report data from their centre's longitudinal follow-up (for up to 10 years) of women with a diagnosis of PCOS, concomitant overweight/obesity, and normal glucose handling at baseline.

From the data collected from 159 women, there was evidence that metformin had beneficial effects on body weight and glucose homeostasis, plus improved androgen levels and menstrual regularity. However, whilst significant adverse effects were not observed, long term adherence to metformin treatment was low, with >75% of patients having discontinued metformin by 5 years, and only 6% of patients still on metformin after 10 years.

Read the full article in *Endocrine Connections* 9 44–54

ENDOCRINE HIGHLIGHTS

A summary of papers from around the endocrine community that have got you talking.

Bio-ink promises 3D printing of functional human ovaries

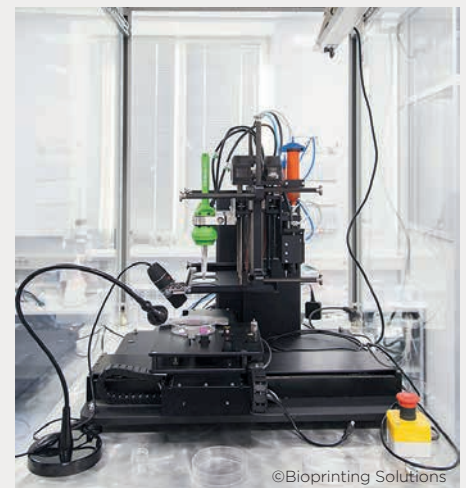
Primary ovarian insufficiency (POI) and early menopause are serious off-target effects, affecting approximately 1 in 6 of female cancer survivors. POI has a plethora of biological effects beyond fertility, and is associated with an increased risk of several comorbidities, as a result of a lack of ovarian hormones. Previous work in ovariectomised mice has shown that ovaries created using 3D printed gelatine scaffolds have successfully restored hormone production and fertility. However, there is a need to understand the native microenvironment and move towards translation for human use.

Henning *et al.* recently published work detailing the development of a bio-ink for 3D printing bioprosthetic ovaries. Pig ovaries have the same

structural proteins as those found in human ovaries, and the locations of structural proteins were identified and imbued into the bio-ink, resulting in an abundant source of proteins to create a complex bio-ink for 3D printing human ovaries. The use of such technology creates the possibility of 3D printing of artificial ovaries that have the potential to be implanted into infertile women, to restore their fertility.

This exciting research aims to use ovarian structural proteins to engineer a biological scaffold capable of supporting a bank of potential eggs and hormone-producing cells. It is envisioned that upon implantation, the artificial ovary could respond to natural cues for ovulation, so enabling pregnancy.

Read the full article in *Scientific Reports* 9 20001
<https://doi.org/10.1038/s41598-019-56454-3>



EXPLORING ENDOCRINE PHYSIOLOGY DURING ARDUOUS EXERCISE

WRITTEN BY SQUADRON LEADER ROBERT M GIFFORD AND COLONEL DAVID R WOODS



Exercise is associated with metabolic and cardiovascular benefits for most people, but do positive physiological adaptations occur when exercise is pushed to extreme limits?

'Arduous exercise' can imply very strenuous physical activity, or exercise made challenging for other reasons, such as climactic exposure, psychological stress or sleep deprivation. What is arduous is also relative to an individual's physical condition – the average patient attending a type 2 diabetes clinic and an Olympic rower are likely to perceive this very differently.

Most people planning to undertake extremes of exercise are healthy and physically fit, so studying them allows us to define the limits of what we consider to be healthy physiological adaptation. Studies of extremely arduous exercise are often observational, field-based and opportunistic for ethical reasons. For example, the intrinsic dangers of ascent to high altitude or crossing the Antarctic must be accepted by participants prior to the additional ethical considerations of participating in research.

HORMONES IN EXERCISE

Hormones are the key mediators of physiological adaptations to exercise, for example by improving metabolic risk from increased insulin sensitivity, increasing muscle mass by upregulating insulin-like growth factor-1, or improving bone mineral density by favouring bone deposition over resorption. However, at sustained extremes of training, some hormonal changes may be considered maladaptive, e.g. catecholamine and/or glucocorticoid excesses thought to mediate overtraining syndrome, impaired spermatogenesis or ovulatory dysfunction during extremely arduous training, or osteopenia and stress fractures seen in ballerinas and distance runners.

THE CONCEPT OF 'ENERGY AVAILABILITY'

Workers in the field have long focused on the balance of caloric energy and its effects on endocrine axes during arduous exercise, specifically the concept of low 'energy availability'. This is the energy available to cellular processes after exercise energy expenditure is subtracted from energy intake, expressed as kcal/kg lean body mass per day. The concept of low energy availability has gained traction as being central to many putative negative endocrine effects of highly arduous training.¹ A value below 30 kcal/kg per day is often considered 'low', although studies have demonstrated a dose-response relationship between energy availability and some maladaptive effects of exercise.²

The 'female athlete triad' comprises reduced bone mineral density and/or hypothalamic-pituitary-gonadal (HPG) axis function due to low energy availability. Downregulating less important processes like bone turnover and reproduction is thought to be a temporary adaptation, limited caloric energy is apportioned to physical activity (e.g. escaping a threat or finding food), as this is of greater importance to immediate survival. Downregulation of certain processes in the context of nutritional deficit should therefore be regarded as an adaptive process and not a pathological one. Sustained low energy availability has been proposed as the cause for a wide array of metabolic and endocrine disturbances during arduous exercise, the 'relative energy deficiency in sports' syndrome, and affects both men and women.

These paradigms may present the correction of low energy availability as a panacea for mitigating endocrine maladaptation to arduous exercise. While this carries the advantage of being modifiable, the evidence largely comes from professional or semi-professional athletes, and it may be that a single aetiology cannot explain arduous exercise-associated maladaptation in other populations. Clinicians and researchers should keep an open mind as to other causes of observed hormonal perturbations. For example, HPG

or hypothalamic-pituitary-adrenal (HPA) axis dysfunction could be due to psychological stressors during arduous exercise. We studied 52 women undertaking highly physically demanding Army training, in whom energy availability was sufficient, but suppression of ovulation and pituitary gonadotroph function was pronounced, associated with activation of the HPA axis.³ These effects were probably due to a combination of multiple stressors, including sleep deprivation and externalised locus of control.

EXAMINING GENDER DIFFERENCES

Studying highly arduous training raises intriguing possibilities of understanding the effects of basic biological covariates like sex on physiological adaptation. It has been reported that the female HPG axis is more sensitive to the effects of low energy availability than the male axis during sustained arduous training.⁴ Women utilise proportionately more lipid and less carbohydrate than men during prolonged exercise, which may mean they are naturally better-adapted to endurance exercise, and preserve lean mass during ultra-long distance races or expeditions. Elite women athletes have dramatically narrowed the gap in a number of endurance sports.⁵

Gender differences in psychological resilience could also be important. We found that six women who crossed Antarctica, each hauling 80kg over 1000 miles in austere conditions, had rates of psychological stress that were lower during the expedition than beforehand. They demonstrated preserved dynamic HPG and HPA axis function, despite an overall energy deficit (around 10kg loss in fat mass).⁶

THE BENEFITS OF COLLABORATION

Research in the field of 'arduous exercise', from bench to mountainside, stands to benefit from greater collaboration between physiologists and endocrinologists. Combining the disciplines in a symbiotic approach can refine the questions and finesse the research outputs. Such cross-talk between disciplines and the study of the human physiological and endocrinological responses to extremes of environmental and exercise exposure can serve to optimise the translational benefit.

Exercise at high altitude induces hypoxic and inflammatory responses akin to systemic inflammatory response syndromes seen in intensive care. Brain natriuretic peptide (BNP) and N-terminal pro-BNP, with which many clinicians will be familiar as supporting a diagnosis of heart failure, have been found to be markers of high pulmonary artery systolic pressure at altitude (a key feature of high altitude pulmonary oedema), while copeptin has been found to reflect thermal strain. Prolonged arduous training with sleep deprivation or psychological stress may be relevant to understanding endocrine dysfunction in highly demanding occupations.

Measuring detailed endocrine function during arduous exercise is extremely challenging, and has been limited by difficulty in obtaining samples during or close to extreme exercise. Wearable technologies, which can perform an increasing number of real-time assays and other measurements, have the potential to improve our understanding of endocrine adaptation to arduous exercise. Continuous accelerometers, cardiac monitoring using ECG or plethysmography and interstitial glucose monitoring systems are already in clinical use, and have been used in extreme environments, delivering continuous real-time data to smartphones. Engineers have developed wearable and implantable sensors of steroid hormones and electrolytes which can last weeks or months.

These innovations are not without ethical challenges in the research and clinical setting. How does one respond to real-time data that suggest an individual is recording measurements out of the conventional 'normal range', when perhaps, in a remote or dangerous environment, extreme values might just be 'normal for them'? A peripheral oxygen saturation of 75% is commonplace at high altitude, but would warrant urgent intervention

in the ward-based clinical setting. It is likely that our physiological ‘models’ of adaptation to arduous exercise are limited by reference ranges taken in non-exercising individuals.

Engaging endocrinologists, physiologists and engineers to develop new technologies presents the opportunity to explore the limits of adaptation to extremely arduous exercise, while bringing the challenge of understanding the physiological versus the pathological.

**SQUADRON LEADER ROBERT M GIFFORD AND
COLONEL DAVID R WOODS**
University of Edinburgh

EXERCISE: WHAT ARE THE METABOLIC BENEFITS?

WRITTEN BY DAVID DEARLOVE, SIÓN PARRY AND LEANNE HODSON



A new year often brings new resolutions. Does ‘I’m going to exercise more this year’ sound familiar?

Often the main goal is to lose weight or more specifically, lose fat. (In this regard, Meerman and Brown provide an interesting insight into ‘When somebody loses weight, where does the fat go?’¹) Based on the weight loss model of ‘calories in verses calories out’, undertaking regular exercise should help with this goal, although evidence shows that exercise alone may not be sufficient.²

Independent of weight loss, it is an incontrovertible truth that exercise is healthful. Any level of activity is associated with a 20% lower risk of mortality – even when it doesn’t reach the minimum national guidelines.³ So, what types of exercise should we be doing? At a basic level, we should undertake a combination of aerobic and strengthening activities.

AEROBIC ACTIVITY

Aerobic activity is often talked about in terms of intensity. The current NHS guidelines state ‘at least 150 min of moderate aerobic activity or 75 min of vigorous aerobic activity per week’. These have recently been updated to say ‘you can also achieve your weekly activity target with several short sessions of very vigorous intensity activity’. Moderate, vigorous, very vigorous – what do these mean? And does intensity really matter?

There are no universally accepted biochemical or physiological markers to distinguish between ‘light’, ‘moderate’, ‘vigorous’ and ‘very vigorous’ exercise intensities. Percentage of maximum heart rate is most commonly referred to; however, this is not always a reliable measure.⁴ Given its subjective nature, and the fact not everyone has or wears a heart rate monitor, then perhaps the best method to gauge exercise intensity is through perceived exertion (see Table).

There is a linear relationship between energy expenditure (EE) and the intensity of exercise performed: the harder you work the more calories you burn (Figure 1). You’d have to exercise for approximately twice as long at a light–moderate intensity (~35% maximum) to burn the same number of calories as at a very vigorous intensity (~85% maximum).

REFERENCES

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5. Lepers R 2019 *Frontiers in Physiology* **10** 973.
6. Gifford RM *et al.* 2019 *Medicine & Science in Sports & Exercise* **51** 556–567.

THE UNDERLYING BIOCHEMISTRY

Given this, if your goal is weight loss, do you only need to exercise at a very vigorous intensity? Not necessarily, as at a very vigorous intensity your body is almost entirely reliant on carbohydrate (CHO) oxidation (mostly glucose derived from muscle glycogen) through mitochondrial and cytosolic glycolysis. Cytosolic glycolysis is a proton-producing pathway (contrary to widely held beliefs, these protons are not derived from the production of lactic acid⁵). Very approximately, the point at which you become entirely reliant upon glucose, with an increasing contribution to energy production

Table. Exercise intensity based on perceived rate of exertion

Category	Rating	Rating of perceived exertion	Guide
Light	6	No exertion	
	7	Extremely light	
	8		Can sing
	9	Very light	
Moderate	10		
	11	Light	
	12		Can talk but not sing
	13	Somewhat hard	
Vigorous	14		
	15	Hard	
	16		Can’t speak in full sentences
	17	Very hard	
Very vigorous	18		
	19	Extremely hard	Maybe an occasional grunt!*
	20	Maximal exertion	

*Please note that this is an unofficial definition, but this is about all you can get out at that intensity!

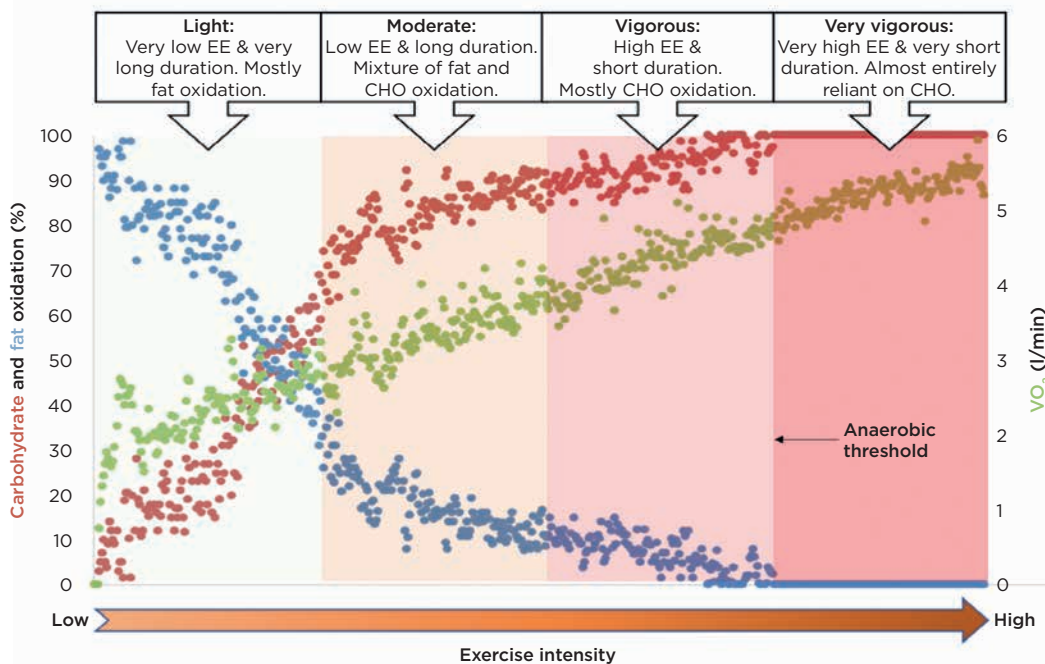


Figure 1. Energy expenditure (VO_2) and substrate utilisation during an incremental intensity exercise test. CHO, carbohydrate; EE, energy expenditure; VO_2 , volume of oxygen consumed (used as a proxy for EE).
● CHO; ● fat; ● VO_2 . ©D Dearlove

from cytosolic glycolysis is referred to as the anaerobic threshold. Exercise above this threshold is painful and as such, cannot be sustained for extended periods. So, whilst you may be burning more calories, you cannot exercise for as long.

In contrast, if you exercise at moderate intensity (utilising a mixture of fat and CHO as substrates), you can keep going for longer and you need to ‘go for longer’ to burn the same number of calories. Indeed, longer duration, moderate intensity exercise and shorter duration, very vigorous exercise appear to be similarly efficacious for reducing body fat percentage.⁶

Regardless of the intensity, try to avoid consuming sports drinks whilst exercising. Even the leanest individual has enough fat to fuel low–moderate intensity activity for hours. Whilst CHO stores are more limited, unless you’re planning on exercising at a vigorous intensity for over an hour, sports drinks are still not necessary.

STRENGTHENING ACTIVITY

NHS guidelines also advocate muscle-strengthening activities such as lifting weights, typically called resistance training. Increasing and/or maintaining skeletal muscle mass is an important mediator of metabolic health, due to skeletal muscle’s prominent role in determining basal metabolic rate, mobility and stability.⁷

The regulation of skeletal muscle mass is determined by the balance between muscle protein synthesis (MPS) and muscle protein breakdown (MPB).⁸ Resistance exercise increases MPS for 24–48h, although net protein balance remains negative without protein/amino acid consumption.⁹ For the majority of individuals, sufficient protein can be consumed through dietary sources, rather than requiring specific supplements. Indeed, it has been reported that self-prescribed, spontaneous use of protein and CHO supplements by amateur men undertaking resistance training at gyms had no positive effects on body composition, compared with individuals who were not taking supplements.¹⁰

Guidelines regarding the optimal resistance training programmes to gain strength and build muscle are available.^{11,12} However, resistance exercise constitutes any action of skeletal muscle against external resistance, and

therefore includes carrying heavy shopping bags or children, and activities such as digging in the garden. These latter options may be preferable introductions to resistance exercise for those who are less familiar/confident in the weights room.

WHAT ABOUT OTHER METABOLIC BENEFITS?

Undertaking a combination of aerobic and strengthening activities is encouraged, and there are many metabolic benefits to be gained from all forms of activity (Figure 2). For example, compared with moderate intensity exercise, vigorous to very vigorous exercise may increase VO_{2max} (the maximum volume

of O_2 taken up per minute – an excellent indicator of metabolic health),¹³ result in greater or comparable improvements in insulin sensitivity and glycaemic control¹⁴ and cause larger decreases in systolic blood pressure.¹⁵ However, further work is required to determine whether a particular type/intensity of aerobic exercise is truly superior for long term health outcomes.

Strengthening activities aid in the regulation of glycaemic control and fatty acid oxidation. Indeed, an increased ratio of skeletal muscle to total body mass is inversely associated with cardiovascular disease risk, insulin resistance and type 2 diabetes.^{16,17} This becomes even more important with age, due to the gradual decline in muscle mass and strength that

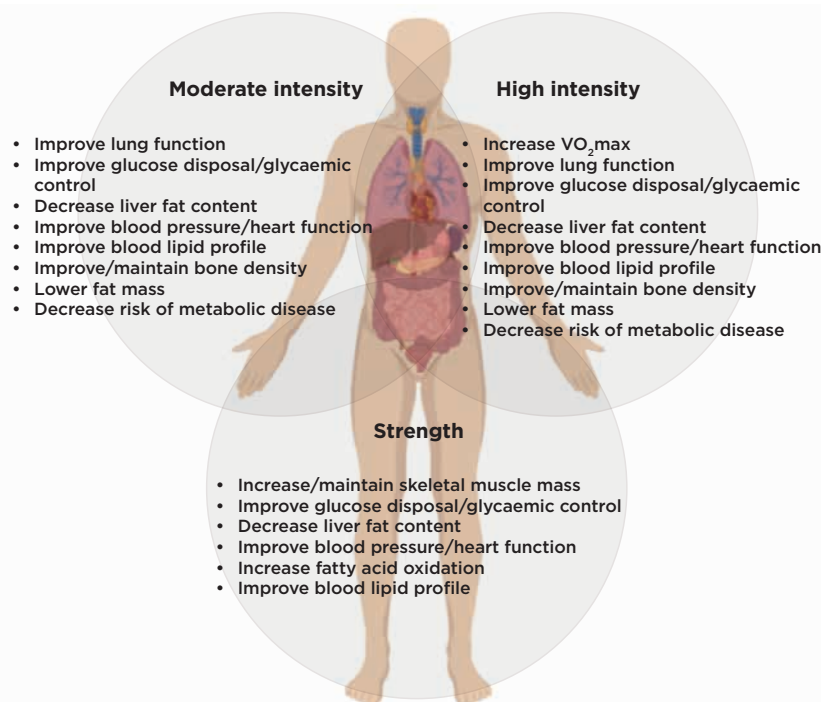


Figure 2. Overview of some of the metabolic effects of moderate intensity, high intensity and strengthening physical activity. VO_{2max} , the maximum volume of O_2 taken up per minute. ©L Hodson

accompanies ageing (i.e. sarcopenia). This is associated with an increased risk of falls, disability and overall mortality.¹⁸

IN CONCLUSION

As the age-old saying goes, ‘every little helps’ – but to get the metabolic benefits of physical activity/exercise it needs to be undertaken regularly. Habit forming (and maintaining) is hard work but, as discussed, adding structured activity to your daily life has many health benefits.

Find what you enjoy and stick at it. If you are breathing a little harder or your muscles are straining, it’s almost certainly going to be having a beneficial effect.

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TYPE 1 DIABETES AND EXERCISE

WRITTEN BY TAFFY MAKAYA AND STEFAN HAEST



Consultant Taffy Makaya and patient and keen sports participant Stefan Haest consider the issues faced by individuals with type 1 diabetes (T1DM) when taking part in physical activity.

WHY IS EXERCISE IMPORTANT IN TYPE 1 DIABETES?

The importance of exercise in maintaining health and well-being in people living with T1DM is well recognised.^{1–3} Extensive research has shown that there are many health benefits to physical activity, sport and exercise in children, young people and adults living with T1DM^{4–7} and these include:

- reduction in long term cardiovascular disease risk
- reduced insulin resistance
- improved blood pressure and endothelial function
- reduced risk of diabetic retinopathy
- reduced glycated haemoglobin (HbA1c)
- improved fitness and sense of well-being.

ACKNOWLEDGING THE CHALLENGES

However, managing T1DM and exercise is challenging. As a result of this, people with T1DM are generally less active than their peers who do not have diabetes⁸ and people living with T1DM have highlighted several obstacles which limit them from engaging in sport. In addition to the barriers reported by the general population, surveys of people with T1DM highlight a number of additional limitations:^{9–11}

- fear of hypoglycaemia
- worrying about poor performance or under-performance when blood glucose readings are high
- lack of confidence in managing diabetes around sport/exercise

- difficulty in engaging in spontaneous exercise, due to a need for planning around diabetes.

People with T1DM involved in high level sports, competitive sport or endurance training may experience these concerns more severely or more frequently.¹² These athletes train regularly, often for long sessions, and may take part in competitions and tournaments.¹² Calculating nutritional and fluid requirements in very active athletes can also be challenging.^{13,14} It is important to consider the energy needs for the basal metabolic rate and also the increased demands for the training and exercise.^{15,16} This is particularly challenging for younger athletes who are still growing, or athletes trying to maintain a particular weight for ‘weight category sports’ or endurance sports like marathon running, or building muscle bulk/strength for power-based sports.

MOVING FORWARD

Over the past 20 years, there have been significant developments in theories regarding the impact of different types and intensities of exercise on blood glucose levels in this population. There are also newer technologies, such as continuous glucose monitoring systems, which (in addition to faster-acting insulins and insulin pumps) can provide real-time monitoring of interstitial glucose levels, and more precise adjustments to insulin doses before, during and after activity.¹⁷ Technology is also moving towards a ‘closed loop’ system

'People living with T1DM have highlighted several obstacles which limit them from engaging in sport.'

for diabetes management. This has allowed the development of evidence-based exercise and physical activity consensus guidelines for individuals with type 1 diabetes, which are definitely worth a read.^{18,19,20}

In addition, several centres now provide dedicated 'diabetes sports clinics' or 'sports consultations' to help support this population of athletes.^{21,22}

IN SUMMARY

Despite the many challenges, particularly fear of hypoglycaemia, engaging in sport and exercise is important for health and well-being in people living with T1DM. There have been many advances in technology and specialist guidance, which now make it easier and safer for people with T1DM to feel more confident about taking part in sport, exercise and endurance challenges. It is important for anyone living with T1DM to have the support of healthcare professionals and peers in developing a sense of independence in managing diabetes and sport.

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PATIENT PERSPECTIVE *by Stefan Haest*

I was diagnosed in 2003 at the age of 9, and have now had diabetes for 16 years. My mother noticed classic symptoms, such as frequent drinking and wetting the bed. I lost weight, and tackles in rugby began to hurt more. After a golf coaching session, I spent my pocket money on a Fanta and a Snickers bar and, later that day, I was diagnosed with a blood glucose level of over 40mmol/l, although ketones were very low.

Since diagnosis, I have been on twice daily mixed insulin, basal/bolus, insulin pump at age 16, and now pump with use of flash/continuous glucose monitoring. I have moved schools and geographical areas for university, and been diagnosed with coeliac disease and hypothyroidism.

I have always played sports, whether in school lessons, the playground or at club level. After my diagnosis, none of this changed. I was taught to do a finger-prick test before, during and after, and have carbs pre-sport and then if I were low. After diagnosis, I took 1 week off from local club rugby, but was back the following week. Exercise was normalised back into life immediately.

As has been widely documented, exercise has profound health impacts on key metrics for T1DM, such as HbA1c. However, it has impacts on mental and social aspects of life. Overcoming the challenges of managing diabetes is complex, and motivations or fears vary with each individual. Although a certain level of fear of hypoglycaemia is present when doing exercise, the larger fear for me, as a child, was a fear of missing out or a feeling that 'you can't'. I believe children naturally wish to play, engage and have fun with their peers. It has been important not only for my diabetes management, but also for my personal development, that I have had the ability and confidence to build up my own experience of various

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sports at various levels: skiing trips, being a badminton coach, club hockey, club and 1st XV rugby, cycling at university and club level, weight-lifting etc.

I have completed different challenges, mainly long distance cycling events (100 miles+) and others, such as a trail race up and down Snowdon. My next goal is to complete a 70.3 Ironman (a long-distance triathlon). As I have begun to increase the frequency and competitive nature of the sport I do, it has forced me to increase my knowledge and experience of nutrition, and search out knowledgeable healthcare professionals and 'diabetes sports clinics'. Although challenging, I view this in a positive sense as, although I have to pay attention to this more due to my T1DM, it has also led me to have a strong knowledge of my body, fueling and how to perform better.

I have volunteered with the Oxfordshire Paediatric Diabetes Service for 7 years to educate children with T1DM and their parents about managing a healthy life with regards to school, sport and lifestyle. Notably, this has entailed practical residential sports activity weekends and Q&A evenings. I do this to demonstrate that nothing is off-limits. In my experience, it is often beneficial to learn from peers with shared understanding and experience, regardless of how good healthcare professionals may be.

In my experience, confidence and independence with sport and T1DM are created by means of three key things:

- a) a good basic understanding of the physiological mechanisms
- b) practical trial and error experience, with the application of theoretical understanding into strategies
- c) preparedness.



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EXERCISE AND ENDOCRINOLOGY IN ADVANCED AGE WITH A FOCUS ON TESTOSTERONE

WRITTEN BY LAWRENCE HAYES



Ageing is experienced by us all, yet we age at a non-uniform rate. Our physiological and endocrinological age may not be reflected by our chronological age, or the number of candles on our birthday cake.

AGEING WELL: WHY IT MATTERS

Recent history has seen an explosion in human longevity in the western world. In less than 200 years, the UK's average lifespan has doubled from 40 to 80 years of age, a trend which has been mirrored in Western Europe and Scandinavia. These numbers would be unimaginable to prior generations and, as technological and medical research advances, we question how much further human lifespan can increase.

Whilst lifespan has increased over several decades, health span (the phase of life without disability and free from serious chronic diseases) has not. The difference between health span and lifespan is not merely one of semantics, but has profound implications for health services worldwide.

As an example, the UN estimated that 3,376,000 people in the UK were over 80 in 2017, which will rise to 7,506,000 by 2050. If these individuals are healthy, they will continue the activities of daily life unassisted. However, if these octogenarians, nonagenarians and centenarians pursue a sedentary life, they may have a level of functional ability (the ability to go about activities of daily living) which is too low to maintain independence (see Figure).

The repercussion of this is institutionalisation, and potentially nursing care. The average cost of a residential care home with nursing is approximately £40,000 per person per annum in the UK. On an individual basis this is extremely costly, but on a national level this could be crippling.

HALLMARKS OF HUMAN AGEING

Biological ageing is characterised by a progressive loss of physical function and an increased risk of developing various common diseases, including cardiovascular disease, type 2 diabetes and many cancers.¹ Yet, heterogeneity exists in many hallmarks of ageing, including telomere length,² the hormonal milieu³⁻⁵ and physical function.⁶ That ageing occurs at a non-uniform rate provides hope, suggesting there

are modifiable factors that can increase lifespan and health span alike. We can observe this in everyday life, as some nonagenarians appear to have the physiology of a sexagenarian, and some sexagenarians are already frail, and exhibit the body of someone far older than their chronological age.

EXERCISE AS A COUNTERMEASURE TO AGEING

A major obstacle to achieving increased health span, reduced morbidity, and optimal longevity in older individuals is the decline in physiological function that accompanies advancing age.⁷ Thus, lifestyle interventions capable of offsetting biological ageing will prolong the health span.⁸

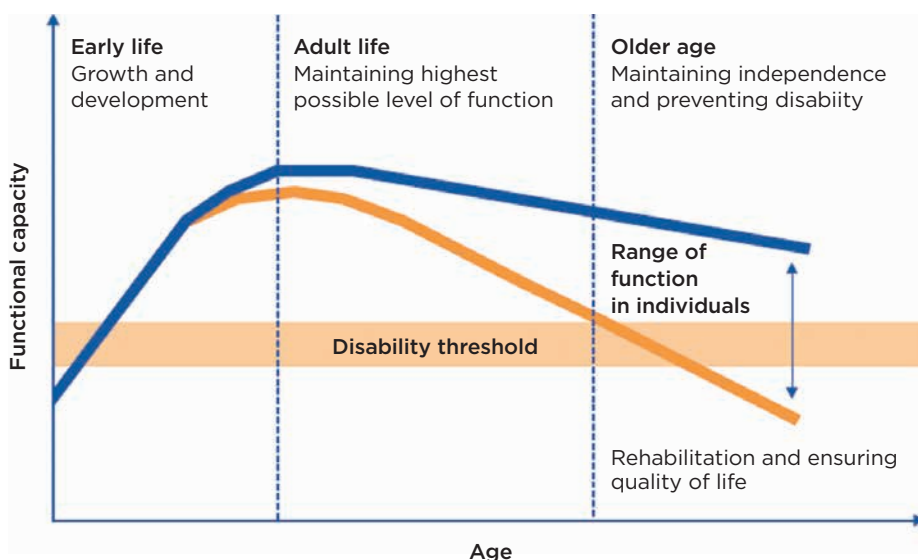
One such strategy is physical activity and/or exercise. This has been proposed as a countermeasure to biological ageing, whereby physically active humans are phenotypically younger than sedentary counterparts, or where individuals display a 'younger' phenotype after exercise training.⁹⁻¹⁴ If we take the classic hallmarks of ageing as reduced physical functions, it is clear that exercise can increase muscle mass and strength, reduce frailty and increase cardiorespiratory fitness.¹⁵⁻¹⁷

HALLMARKS OF ENDOCRINE AGEING

Much like circadian rhythms, rhythms of the menstrual cycle and seasonal variations in hormones, hormonal concentrations vary throughout the life cycle. Indeed, one programmed theory of ageing posits that changing hormonal secretion over our lifetime is causative in the ageing process.

For example, testosterone peaks at puberty in males and declines gradually from the fourth decade of life onwards.¹⁸ As testosterone is implicated in the maintenance of healthy metabolism and muscle and bone health, amongst other factors, this decline of the primary male sex hormone has been suggested as a reason for age-related reduction in physical functioning. As a result, testosterone supplementation has garnered interest for its rejuvenative potential.¹⁹ This can also be applied to growth hormone (GH) and other 'anabolic' hormones.²⁰

Figure. A life course perspective for maintenance of the highest possible level of functional capacity (source: WHO/HPS, Geneva 2000). © WHO/HPS



This poses the obvious question, if we reverse the tide of endocrine ageing through exogenous supplementation of these hormones, can we retard human ageing? Storer and colleagues demonstrated that 3 years of testosterone supplementation prevents the age-associated decline in muscle mass and function.¹⁹ This has been supported by Atkinson *et al.*, who observed that 6 months of testosterone supplementation mitigates age-related loss in muscle (sarcopenia).²¹ Therefore, if we avoid endocrine ageing, some aspects of whole-body human ageing can be augmented. However, there are many issues associated with exogenous administration of testosterone, particularly cardiovascular events.²²

EXERCISE AS A COUNTERMEASURE TO ENDOCRINE AGEING

As previously mentioned, hormones exhibit a common pattern over the life course. In females, menopause represents the major turning point in the hormonal milieu. Yet, in males the decline in ostensibly anabolic hormones is more gradual.

In the normal population, a progressive fall in GH secretion occurs with increasing age and is reflected in a parallel fall in circulating insulin-like growth factor-I (IGF-I). This fall is termed the 'somatopause',²⁰ whilst the age-related reduction in testosterone is termed the 'andropause'.²³

It is of interest to know whether exercise can be prescribed as a first line treatment for falling 'anabolic' hormones. Several research groups have sought to answer this question, with varying results. For example, Maass *et al.* observed no change in GH or IGF-I following 3 months of aerobic training in older adults²⁴, and Arnarson *et al.* reported a reduction in serum IGF-I following 12 weeks of resistance training in elderly adults.²⁵ However, we have previously reported that male masters athletes (competitive athletes over 60 years of age) exhibit greater IGF-I concentrations compared with lifelong sedentary counterparts. Moreover, after high intensity interval training (HIIT), both groups experienced an increase in IGF-I (to a larger extent in the previously sedentary group).²⁶ Similarly, we have observed this increase in IGF-I (and GH) in middle-aged individuals following an intensive training period.²⁷ Therefore, it seems likely that a lifetime of exercise, and short term exercise training of sufficient intensity, can maintain somatotrophic hormones compared with sedentariness.

With regards to testosterone, the picture is somewhat murkier. In a recent meta-analysis, the influence of short term exercise (i.e. up to 1 year) on basal testosterone in older males was examined, and there was little effect of resistance training or endurance training on any testosterone fraction in the ageing male.²⁸ With regards to lifelong exercise habits, we have shown that endurance-trained masters athletes and sedentary older adults exhibit similar total testosterone, bioavailable testosterone and free testosterone.¹⁰

However, an interesting preliminary finding was that more of the sedentary individuals were classed as biochemically hypogonadal (clinically low total testosterone) than was the case for the masters athletes.²⁹ This may suggest that lifelong exercise does not increase a group mean testosterone, but may protect against clinically low testosterone (possibly via avoidance of obesity and the effects of excess adiposity). When we subjected these individuals to HIIT, both the previously sedentary group and the masters athletes increased free testosterone (purportedly available for tissue uptake), but not total testosterone.^{30,31} Thus, HIIT appears to have the most promise with regards to increasing basal testosterone in the short term, yet much more research is required to confirm this.

'The complexity of the endocrine system makes this area of study simultaneously fascinating and challenging.'

CAN EXERCISE REVERSE THE TIDE OF (ENDOCRINE) AGEING?

This depends how we define ageing. If ageing is merely the passage of time, then probably not. However, if human ageing is associated with physical inactivity (which at present it is³²), then the answer is probably yes. Active older individuals, particularly masters athletes, have a greater physiological capacity than sedentary older adults.³³

With a focus on testosterone, whether exercise can prevent or reverse the andropause is unclear. However, I must stress that, despite most of my research into the endocrinology of ageing and exercise being focused on testosterone, this is only one factor in the hormonal milieu, and exercise is efficacious at improving other hormonal variables associated with successful ageing.^{3,26,27}

At present, exercise is probably our best countermeasure (in terms of avoidance of side-effects) to endocrine ageing and whole-body ageing.

CHALLENGES AND SCOPE FOR FUTURE RESEARCH

There is still so much we do not know about the influence of exercise on ageing endocrinology. The complexity of the endocrine system makes this area of study simultaneously fascinating and challenging. One issue in interpreting findings concerning testosterone and exercise is that there are several upstream and downstream intermediary hormones implicated in the hypothalamic-pituitary-gonadal axis. Moreover, measurement of sex hormone-binding globulin is required (if equilibrium dialysis is unavailable) to measure free testosterone (the hormone fraction available for tissue uptake). Likewise, measurement of tissue androgen receptor number is needed for an understanding of whether testosterone can exert an effect at the tissue level.

Advances in physiological research methodologies, particularly the popularisation of the biopsy technique and high sensitivity detection methods, will hopefully shed light on these topics in years to come.

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STRONG, STEADY AND STRAIGHT: EXERCISE RECOMMENDATIONS FOR OSTEOPOROSIS AND BONE HEALTH

WRITTEN BY SARAH LEYLAND AND JON TOBIAS



The Royal Osteoporosis Society (with support from organisations such as the Society for Endocrinology) has worked with scientists and clinicians in the field of osteoporosis and bone health to produce a consensus statement¹ on the role of physical activity and exercise for osteoporosis, with new information resources for patients.² This publication will help clinicians advise their patients with osteoporosis more appropriately and confidently. New information clarifies the types of exercise that will help patients optimise their bone health and reduce their risk of fragility fractures.

WHY A CONSENSUS STATEMENT?

Patients with osteoporosis often ask what exercise they should do to reduce their risk of fracture, and how safe this is. We frequently encourage weight-bearing exercise, while discouraging bending forward, to reduce the risk of vertebral fractures. If we are honest, we aren't too secure or confident in

our response, and patients have probably gone away somewhat confused and maybe fearful about what they should and shouldn't do.

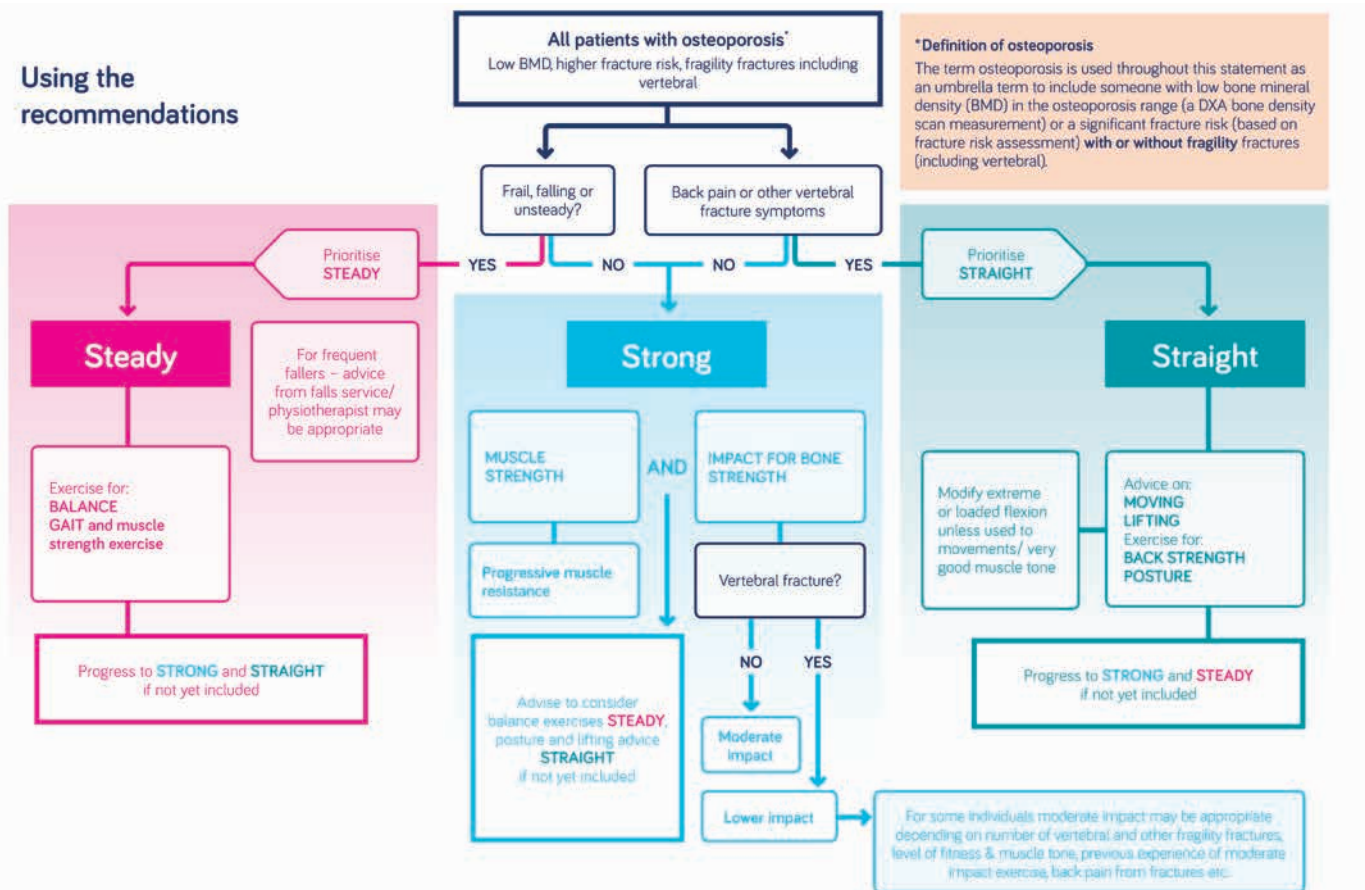
Royal Osteoporosis Society helpline reports, surveys and stakeholder group meetings not only confirmed that these experiences were common, but also found, worryingly, that patients often do less exercise and activity after their osteoporosis 'diagnosis'.³⁻⁵

This uncertainty and confusion about the effectiveness and safety of physical activity and exercise in promoting bone strength and reducing fracture risk in patients with osteoporosis prompted the Royal Osteoporosis Society to produce a consensus statement. The aim was to improve professionals' knowledge and practice and, consequently, the care and advice received by patients.

DEVELOPING THE STATEMENT

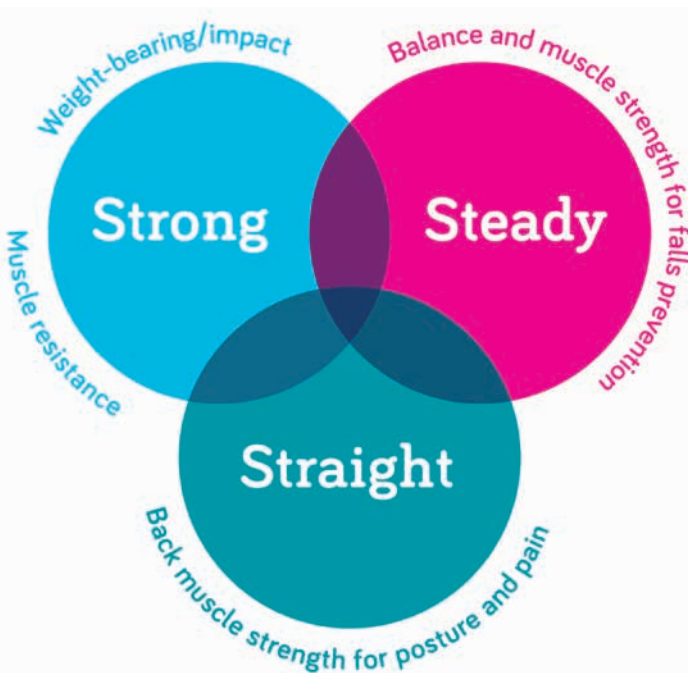
Experts, including scientists, academics, health and exercise professionals, and patient representatives were invited to examine the evidence and commission further evidence reviews. Since comprehensive evidence reviews had recently been completed,⁶⁻⁸ a further systematic review was not felt necessary. Instead, a review was commissioned to 'fill the gaps', especially in relation to 'exercise harms'.⁹ The group aimed to reach an expert consensus in those frequent instances where evidence was limited, with the intention of making positive recommendations where potential benefits were considered to outweigh harms.

The *Strong, Steady and Straight Quick Guide*, including this flow chart to tailor exercise information for patients, can be downloaded at www.theros.org.uk/media/100224/royal-osteoporosis-society-strong-steady-straight-quick-guide.pdf.



THEMES AND RECOMMENDATIONS

The consensus statement identifies three themes under which being physically active and taking exercise can help with osteoporosis.



STRONG

Exercise to promote bone and muscle strength

This advice should be integrated with the Chief Medical Officers' recommendations on physical activity for general health.¹⁰ The statement also cautions that exercise should not be a replacement for pharmacological interventions to reduce fracture risk.

Recommendations:

1. Weight-bearing exercise with impact (standing up and moving with some added force) is recommended as follows. About 50 moderate impacts, such as jogs or low level jumps, should be undertaken on most days. For patients with vertebral or multiple other fractures, or for those who are less able, 20 mins of lower impact exercise, such as walking or marching, is recommended. A variety of activities or exercises involving different directions, movements and speeds is ideal. For those who are frail or less able to exercise then, at least, reducing prolonged periods of 'sitting' is recommended (e.g. standing up for a minute or two every hour).
2. Gradually increase the intensity of the muscle resistance exercise. Consider using weights or elastic resistance bands and build up to three sets of 8–12 'repetitions max' (the most you can lift 8–12 times), as part of an exercise programme or activity that works on all the main muscle groups in the body. Advice from a gym or exercise instructor may be necessary in the case of some types of exercise, to ensure safe and effective techniques.

Evidence: There is evidence that being physically active is associated with a reduction in hip fracture risk¹¹ (this may partly be mediated by a reduction in falls risk) and that exercise maintains bone strength, reduces loss of bone mineral density (BMD) and promotes bone strength.^{6,8,12,13}

In terms of the populations that may benefit from exercise interventions, there is some evidence that exercise improves BMD in post-menopausal women.¹² However, more research is needed in older people, especially those with reduced bone strength.⁶ Some recent research has focused on specific types of exercise, such as moderate impact and high intensity muscle resistance exercise undertaken by older women, which led to improvements in BMD.¹⁴

STEADY

Exercise and activity to promote steadiness, so preventing falls and reducing fall-related fractures

Recommendations:

1. Balance and muscle-strengthening exercises are recommended for those over 65 years, or anyone with balance problems, especially before they start new challenging physical activity, such as brisk walking.
2. If patients are already falling, then a referral to a falls service or physiotherapist for a multifactorial falls risk assessment and advice should also be considered.

Evidence: There is good evidence that exercise and physical activity reduce the risk of falls. Most non-vertebral fragility fractures are caused by falls and, in principle, reducing falls risk is likely to reduce fractures. However, more research is needed to confirm that exercise interventions reduce the falls that result in fractures.¹⁵

STRAIGHT

Back-strengthening exercise and safe moving and lifting, to reduce the risk of vertebral fractures and help improve associated symptoms

Though applicable to all patients with osteoporosis, specific recommendations need to be tailored to the individual, taking personal preferences into account.

Recommendations:

1. Consider modifying or finding alternatives to exercises or movements that involve sustained, end range or loaded forward flexion such as 'sit ups' or the 'roll down' in pilates. This is especially important for those without strong abdominal muscle strength, or those who find movements difficult or uncomfortable. These movements have the potential to put increased force or pressure on the anterior vertebral bodies and may increase fracture risk.
2. Back-strengthening exercises are recommended on 2–3 days per week, to help with posture and prevent pain after vertebral fractures (or daily to help with existing pain).
3. Patients with painful vertebral fracture need prompt advice to reduce anxiety levels. They may benefit from a referral to a physiotherapist for a tailored exercise programme.

Evidence: There is some evidence to suggest that exercise may help to improve symptoms¹⁶ and quality of life¹⁷ after painful vertebral fractures.

There is considerable evidence and recognition¹⁰ that physical activity and exercise are important for general health as well as bone health. If people diagnosed with osteoporosis reduce their physical activity because of fears of causing a fracture, this may cause other poor health outcomes.

SAFETY

The consensus statement supports participation in moderate impact exercise, such as jogging and low level jumping, to promote bone strength in patients with osteoporosis. So long as exercise is built up gradually, the risk that this will lead to a vertebral fracture is negligible. Similarly, using weights, even after vertebral fractures, can be useful for improving bone and muscle strength, though it's important that these are tailored to the individual, and that patients are taught good techniques. No specific weight limits or restrictions are recommended.

A more cautious approach is recommended if patients have had vertebral fractures or multiple other fragility fractures, or if they have had a fracture in relation to impact exercise. However, there is no absolute contraindication to moderate impact exercise for these patients. The statement recognises that it may be appropriate for these patients to gradually build up to moderate impact exercise, particularly for those already used to this type of exercise.

Recommendations for safe moving and lifting are based on a principle of 'good preventative measures for all'. They propose that everyone with osteoporosis should learn to 'hip hinge' for safe lifting and moving. Similarly, alternatives or modifications to some types of movement and exercises in pilates, yoga and related activities are recommended.

Generally, a 'how to', positive and encouraging approach by professionals to exercise and physical activity is strongly recommended, both to increase appropriate exercise for fracture risk reduction and management, and to maintain activity for general health.

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The Royal Osteoporosis Society has a free helpline staffed by specialist nurses who are happy to discuss exercise, treatment, pain management and other related issues: Tel: **0808 800035**; Email: **nurses@theros.or.uk**.

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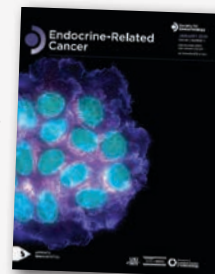


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HYPERANDROGENISM: DIFFERENCES IN SEXUAL DEVELOPMENT AND SPORT

WRITTEN BY PETER SÖNKSEN



We are in an Olympic and Paralympic year, which brings sport to the forefront of life for around 30 exciting days for sport lovers. There are also always controversies. One of the issues currently is how to define hyperandrogenism in female athletes, in particular regarding women with differences of sex development (DSD).

TESTOSTERONE LEVELS IN ELITE ATHLETES

As endocrinologists, we know this is not a straightforward issue for women with DSD. As part of a multi-national European research project, aimed to develop a test to detect growth hormone misuse (GH-2000¹), we collected blood samples from 813 volunteer elite athletes from 4 countries and 15 sporting disciplines. At the end of the project, endocrine profiles were analysed for 693 of these which had enough serum remaining to obtain the profile (454 men and 239 women).^{2,3} Testosterone levels showed some surprising results in both men and women (Figure).

There was a complete overlap between men and women, although the mean values were clearly separate. Of 446 men, 74 (16.5%) had a value below 8.4 nmol/l (the lower limit of the normal reference range), while 32 of 234 women (13.7%) had a testosterone level >2.7 nmol/l (the upper limit of the normal reference range). Those women who had a high testosterone were taller and thinner and had a lower oestradiol level than those with a normal testosterone measurement.

There were 11 women whose testosterone was above 8 nmol/l, one of whom had a low level of luteinising hormone and might have taken exogenous testosterone, but that left 10 of 234 (1:23.4) with a testosterone

level that suggested the presence of the androgen insensitivity syndrome (AIS). Of the 11 women with a testosterone level greater than 8 nmol/l, 2 were rowers, 3 were swimmers and 6 were from track and field.

WOMEN WITH DSD IN ELITE SPORT

It has been shown previously that women with DSD are over-represented in elite sport: at 1:504⁴ and 1:421 at Olympic Games.^{5,6} In these instances, DSD was established genetically, whereas in the GH-2000 series (with the very high prevalence of 1:23), the diagnosis was assumed on the basis of the elevated testosterone level. It is also interesting to note that elite athletes with (presumed) AIS were competing in rowing and swimming as well as in track and field, where all the recent publicity has occurred.

THE 'LEVEL PLAYING FIELD'

This over-representation of women with DSD in sport and its effect on the so-called 'level playing field' is one of the driving forces behind World Athletics (formerly the IAAF) introducing eligibility criteria that restrict access to certain events to women with testosterone levels below 5 nmol/l.

There is good evidence that exogenous testosterone (and anabolic steroids) is a performance-enhancing drug in women,^{7,8} but this is not the same as showing that naturally occurring endogenous testosterone production (as reflected by serum testosterone concentration) in any way determines performance in female athletes. Consultants to World Athletics have exhaustively dredged data from World Athletic Championships looking for correlations between blood testosterone and performance, and have concluded that there is a relationship – but the data are not convincing to me and many others.^{9,10} They were, however, enough to convince two of the three CAS (Court for Arbitration in Sport) judges to allow World Athletics to introduce (yet again) rules discriminating against all the so-called 'hyperandrogenic' female athletes, irrespective of diagnosis.

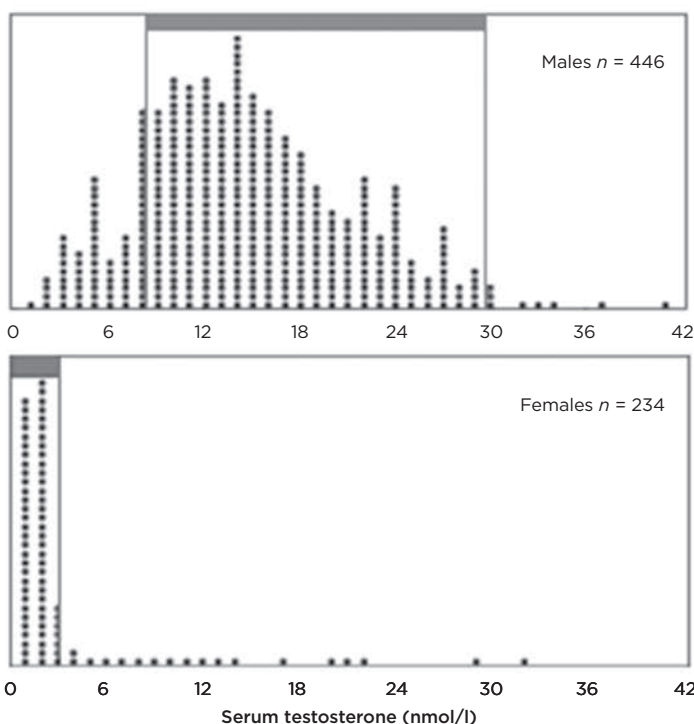
This is grossly unfair, since the largest group of women disenfranchised by this rule are those with complete AIS, who have a defect in the testosterone receptor and cannot respond to any level of testosterone. Their over-representation in elite sport has been attributed to other genes on the Y chromosome that affect characteristics which could themselves affect sporting performance, such as height and lean body mass.⁵

Hopefully, in time, there will be more balanced judgements but, until then, we may not be seeing some talented athletes during the Games in Tokyo 2020.

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Figure. Dot plots of testosterone levels in volunteer elite athletes. ©P Sönksen



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NUTRITION, NAD AND EXERCISE: VITAMIN B₃ SUPPLEMENTS TO STAY FIT AND HEALTHY?

WRITTEN BY ANTJE GARTEN



A diet well-balanced in macro- and micronutrients is the basis for health and well-being. Together with a healthy lifestyle, including physical activity and exercise, it can prevent or postpone the onset of metabolic diseases. Indeed, an increasing number of column-inches are devoted to the latest ways to improve our disease-free life expectancy.¹

Vitamins are taken by millions of people worldwide every day as nutritional supplements, and are a booming industry. One of these supplements, vitamin B₃, is known to be effective against pellagra, a disease caused by malnutrition. Lately, some preparations of vitamin B₃ have garnered huge attention for their seeming ability to counteract symptoms of metabolic disease and ageing decline in preclinical studies.

Let us consider a brief overview of vitamin B₃ metabolism during exercise, and discuss current studies on its supplementation, to see if the hype is true.

FROM VITAMIN B₃ TO NAD

Vitamin B₃ comprises a group of molecules that can act as precursors for the classical enzyme cofactor nicotinamide adenine dinucleotide (NAD), which consists of nicotinic acid (NA), nicotinamide (NAM) and the more recently discovered nicotinamide mononucleotide (NMN)² and nicotinamide riboside (NR).³ NAD is a central mediator of cellular energy metabolism and a crucial link between nutritional intake, cellular metabolism and health.

There are several routes to synthesise NAD. The *de novo* pathway starts from the essential amino acid tryptophan (Trp). Individuals with vitamin B₆ deficiency are not able to sufficiently metabolise Trp,⁴ pointing to the importance of a well-balanced diet with adequate amounts of necessary micronutrients. The different forms of vitamin B₃ are converted to NAD via shorter enzymatic routes,⁵⁻⁷ and can refuel NAD in multiple intracellular compartments, including mitochondria. NMN and NR have been extensively tested in preclinical models for their NAD-boosting capability. They are very efficient at increasing NAD levels in many tissues, while circumventing the undesirable side effects of NAM and NA.⁸

WHY NAD IS NEEDED DURING EXERCISE

NAD and its reduced form NADH have a threefold role in human metabolic physiology. First, they are essential coenzymes in redox reactions, e.g. in energy metabolism. During prolonged exercise, muscles have an enhanced demand for energy in the form of adenosine triphosphate (ATP). Muscle mitochondria start to oxidise increased amounts of fuel: glucose mobilised by glycogenolysis in the liver, and fatty acids from lipolysis in adipose tissue. For both, NAD is required to be reduced to NADH in the tricarboxylic acid cycle, to increase ATP production through the electron transport chain. Indeed, both the levels of NAD and expression of an NAD salvage enzyme in muscle were shown to increase during exercise.^{9,10}

Secondly, NAD is a signalling molecule and substrate for enzymes regulating cellular energy metabolism and stress responses, thereby linking energy metabolism to transcriptional regulation and changes in expression and activity of metabolic regulators. During exercise, ATP is metabolised to adenosine monophosphate (AMP), whilst NADH is concurrently oxidised to NAD to increase ATP production. This state of relative energy deprivation is sensed by master regulators that redirect cellular metabolism to increase fuel for energy production. The AMP-sensing enzyme AMP kinase (AMPK) enhances glucose transport and fatty acid oxidation in acutely exercised

muscle.¹¹ Sirtuins are NAD-dependent enzymes that, together with AMPK, activate the transcriptional coactivator PGC-1 α (peroxisome proliferator-activated receptor- γ coactivator-1 α) during prolonged exercise, which leads to enhanced mitochondrial biogenesis in skeletal muscle^{12,13} and gearing of whole-body energy metabolism towards energy production.¹⁴

Thirdly, the phosphorylated form of NAD, nicotinamide adenine dinucleotide phosphate (NADP/NADPH), plays an important role in oxidative stress defence. An example of this is the requirement for NADPH during exercise, when the increased demand for energy causes enhanced mitochondrial production of reactive oxygen species.

In this scenario, vitamin B₃ could be useful towards refueling depleted NAD levels to meet the increased demand and helping to maintain sirtuin activity.

VITAMIN B₃ SUPPLEMENTATION AND NAD REPLETION

In preclinical models of ageing, nutritional insults (high fat–high sucrose diet, alcohol) and various metabolic disorders such as obesity, type 2 diabetes or fatty liver disease, NAD is often severely depleted to levels that impair redox metabolism and reduce the activity of sirtuins.¹⁵ In numerous studies, repletion of NAD with NR or NMN successfully reversed the negative effects of ageing or diet-induced obesity in mice.¹⁶ The importance of NAD homeostasis in mouse skeletal muscle was shown using a model of genetic depletion, which resulted in decreased muscle strength and endurance exercise performance and could be counteracted by supplementation with NR.¹⁷ The main cause for this beneficial effect was shown to be improved mitochondrial function.^{18,19}

Since NAD repletion was found to be a promising therapeutic route in preclinical models, human clinical trials were started, examining the effects in mildly obese or aged, otherwise healthy, males. NR was found to be a safe way to increase NAD in blood, when applied for short durations,²⁰⁻²² while a clinical trial for NMN focusing on cardiometabolic health has recently been completed.²³ To date, short term NR supplementation in humans is safe and well tolerated; however, in contrast to preclinical models, measures of whole-body energy metabolism, muscle strength and cardiac or endocrine function in humans were not improved.^{20,21,24-28}

COULD NAD REPLETION BOOST EXERCISE PERFORMANCE?

Diets low in micronutrients and vitamins can lead to compromised health through depletion of NAD availability and impaired resilience to metabolic stress. However, until recently, no study had specifically examined whether increased amounts of vitamin B₃, or indeed vitamin B₃ taken as single supplement, are needed or are beneficial during physical activity in humans.

In mice, supplementation with NR was shown to increase exercise capacity, running distance and ATP production in muscle of lean and diet-induced obese mice.¹⁸ Conversely, studies in rats found a decrease in exercise capacity and altered energy metabolism.^{29,30}

In human skeletal muscle, supplementation with NR can augment the NAD metabolome and lead to transcriptional adaptations of energy metabolic genes. A recent study examined exercise performance after NR supplementation in young and old individuals and showed decreased oxidative stress and improved physical performance in old, but not young, subjects.³¹ These data hint towards the need for an individualised approach for NAD repletion only in individuals with pre-existing NAD depletion, which might also be tissue-specific. Carefully designed studies with longer durations, that take into account the type of exercise, will be necessary to tease out potential positive effects of NAD repletion on

exercise performance. Future clinical trials should also address the question of whether muscle NAD levels are actually decreased, as in a recent study including individuals with sarcopenia.³²

IN CONCLUSION

There is no doubt that it is better to consume a well-balanced diet as part of a healthy lifestyle than to consume supplements. Currently, there are limited data or evidence for using vitamin B₃ supplements to increase physical performance or to gain other health benefits in humans. Both athletes and the general public should wait for the results of further clinical trials that are exploring the combined effects of NR supplements and exercise on skeletal muscle and mitochondrial function in healthy individuals³³ or patients with hypertension,³⁴ to determine if NAD repletion could potentially be beneficial for humans.

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JUST DO IT? IS IT SAFE FOR WOMEN TO CONTINUE RUNNING THROUGHOUT PREGNANCY?

WRITTEN BY KATY KUHRT AND ANDREW SHENNAN



An obstetrician we know recently contacted us. She was 30 weeks' pregnant with her first baby, and concerned about her running routine this pregnancy. Before she was pregnant, she ran regularly, and had continued until this point. But, despite browsing the available literature, she felt uncertain as to whether it was safe to keep it up, and was finding it increasingly difficult to justify her continued urge to run in response to family and friends' comments.

This is a typical scenario, which is frequently brought to our attention. Coupled with adverse comments in the popular press about selfish behaviours of women wishing to run, it provided the impetus for us to evaluate the situation further. What should women do if they want to participate in recreational, and even competitive, running during pregnancy?

IN SEARCH OF GUIDELINES

The Royal College of Obstetricians and Gynaecologists' guidelines recommend 150 minutes of moderate intensity exercise each week, in

the absence of obstetric complications,¹ based on evidence of no harm to mother or fetus.^{2,3} But there is limited specific guidance related to running – a more vigorous, weight-bearing activity, which may have unique effects on the developing fetus and female body, antenatally and postpartum. The evidence base is small, with existing studies employing varied methodologies and definitions, making it difficult for health professionals to draw robust conclusions.

Currently, it seems that uncertainty prevails amongst pregnant women who either stop or drastically cut back on antenatal running routines because of

a lack of knowledge surrounding the potential risks, as well as clinicians - in a recent study reporting reasons women stopped running during pregnancy, almost a third did so based on advice from their doctor.⁴

EXERCISE AND BIRTHWEIGHT

Moderate intensity aerobic exercise throughout pregnancy is known to result in a lower caesarean section rate, reduced incidence of gestational diabetes and hypertensive disorders, decreased maternal weight gain and improvements in antenatal and postnatal depression, and has not been found to adversely affect birthweight.⁵⁻⁷

'The evidence base currently suggests that obstetricians can confidently recommend that pregnant women continue to run, and engage in other forms of intense exercise, as long as there isn't a risk of direct trauma to the uterus.'

Studies investigating more intense exercise have reported mixed effects on birthweight, which have potentially important clinical implications, as birthweight is the single most important predictor of neonatal morbidity and mortality.⁸ Decreases in utero-placental blood flow occur during vigorous and high intensity exercise (defined as being at least 70% of maximum heart rate (MHR), or an activity where normal conversation can't be maintained⁹), as blood is redirected towards skeletal muscle. By the third trimester, uterine blood flow has increased from 50ml/minute to 500ml/minute and there are theoretical concerns that regular, strenuous exercise, with associated redistribution of blood flow away from the developing fetus could result in impaired growth or other fetal consequences.

However, a recent systematic review and meta-analysis including 15 studies reported no significant difference in birthweight in infants of mothers who engaged in vigorous physical activity compared with those who didn't. In fact, a Cochrane review of 14 trials (1014 women) reported a reduced risk of large for gestational age (>4000g) and small for gestational age (<2500g) babies, both known to be associated with morbidity.¹⁰ Lower birthweight, on average 200g, was reported for women who exercised into their third trimester, but this reflected reduced fat mass and increased lean body mass,¹¹ which is likely to be associated with better long term health outcomes.

EXERCISE AND PRETERM BIRTH

Running is a weight-bearing exercise, generating considerable forces as the foot strikes the ground, which are transmitted through the limbs and pelvic girdle, with potential contrecoup effects within the uterus that could affect cervical integrity and potentially increase the risk of preterm birth (delivery <37 weeks).

However, no studies have reported an increase in preterm birth, including our own investigation into the running habits of 1293 women during pregnancy, 15% of whom ran into their third trimester. This study was also reassuring, given that recreational and other running was not associated with any detrimental effects on birthweight.¹²

EXERCISE AND ASSISTED BIRTH

General muscle hypertrophy and increased muscle tone attributed to regular exercise could theoretically predispose recreational and elite athletes

to a prolonged second stage of labour and increased assisted delivery rates, related to soft tissue resistance.

We found that the assisted vaginal delivery rate was significantly increased, albeit marginally, in women who continued to run during pregnancy (27%) compared with those who stopped (25%).¹² This may be attributable to hypertrophied and toned pelvic floor muscles blocking the downward passage of the fetus during pushing.

EXERCISING AFTER DELIVERY

The physiological effects of pregnancy are generally thought to persist for 4-6 weeks postpartum and, aside from pelvic floor exercises, women are not typically encouraged to return to strenuous exercise regimes, including running.

However, this is an arbitrary time point, and many women return to exercise earlier, which has been associated with reduced risk of postpartum depression.⁴ In terms of physical effects, theoretically, pelvic floor muscles may be overloaded if they are not fully recovered before a return to strenuous exercise, and early return to heavy physical work after childbirth increased risk of urinary incontinence and pelvic organ prolapse in small populations of women when studied in India¹³ and Nepal¹⁴ respectively. But a consensus statement by Bø *et al.* on exercise in the postpartum period identified no clear evidence of an increased risk of pelvic floor injury.¹³

IN SUMMARY

Continuing to exercise vigorously during pregnancy, including running, does not appear to be harmful to either mother or baby, and this is what we told our colleague. The evidence base currently suggests that obstetricians can confidently recommend that pregnant women continue to run, and engage in other forms of intense exercise, as long as there isn't a risk of direct trauma to the uterus. It also remains likely that exercise in pregnancy has beneficial effects that outweigh any theoretical risks.

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Treating adrenal insufficiency: NEW CROSS-SPECIALTY GUIDANCE

WRITTEN BY JEREMY TOMLINSON AND HELEN SIMPSON



As endocrinologists, we are all aware of the importance of recognising adrenal insufficiency and treating it appropriately. We are familiar with the distinction between primary and secondary adrenal insufficiency and the variety of causes that can lead to the condition.¹

Perhaps less well-recognised amongst specialties outside endocrinology is the ability of prescribed, exogenous steroids to cause suppression of the hypothalamo-pituitary-adrenal axis, leading to so-called 'tertiary adrenal insufficiency'. This can leave the patient vulnerable to the risk of adrenal crisis in exactly the same way as classical primary and secondary adrenal insufficiency.² This is made all the more relevant when we bear in mind the large number of patients who take regular, prescribed glucocorticoid treatment. Most of these patients have never seen an endocrinologist. Such treatments, across all routes of administration (oral, parenteral, inhaled, topical, intra-articular) have the potential to cause adrenal suppression, and this can often be overlooked.³ Whilst there is a lack of prospective evidence to document the risks of adrenal crisis in this group, there is an increased mortality associated with prescribed steroid use, even when correcting for the underlying medical condition.⁴

Adrenal crisis is a life-threatening endocrine emergency, and treatment relies upon the provision of emergency parenteral glucocorticoids, fluid resuscitation and treating any underlying cause.⁵ It can occur in primary, secondary and tertiary adrenal insufficiency and, therefore, rapid and appropriate treatment is fundamental. The National Reporting and Learning System identified 78 incidents, including 2 deaths and 6 incidents of severe harm to patients, in a recent 4-year period, all relating to the omission of steroids during severe intercurrent illness or around a surgical procedure.

'Through the incorporation of this guidance into clinical practice, we hope that patients with adrenal insufficiency (from whatever cause) never suffer an adrenal crisis through lack of administration of parenteral glucocorticoid therapy at the time of surgery.'

Elective surgery is a well-recognised stress. In patients with adrenal insufficiency, it is crucial to ensure circulating glucocorticoid levels are adequate, in order to cope with the physiological stresses associated with the procedure.

A PLACE FOR NEW GUIDANCE

Prompted by a report from HM Coroner into standards of care for patients with adrenal insufficiency, the Association of Anaesthetists of Great Britain and Ireland, the Society for Endocrinology, the Royal College of Anaesthetists and the Royal College of Physicians have come together to produce the first national guidance on the topic that specifically integrates expertise in endocrinology with the practicalities of anaesthetic and surgical services delivery, and addresses the needs of both adults and children.⁶

These guidelines have now been published in the journal *Anaesthesia*, the official journal of the Association of Anaesthetists of Great Britain and Ireland, where it will have broad readership amongst practising anaesthetists.⁶

The key take-home messages include the following:

- prescribed glucocorticoid therapy can cause suppression of the hypothalamo-pituitary-adrenal axis
- all glucocorticoid-dependent patients are at risk of adrenal crisis as a consequence of surgical stress or illness
- patients should be involved in their own care, as they are often well informed; also, work closely with the local endocrine team
- the suggested specific parenteral glucocorticoid regimens depend upon the procedures being performed; these must be tailored in the post-operative period, depending upon recovery and complications
- dexamethasone is not a suitable replacement glucocorticoid as it lacks mineralocorticoid activity
- special considerations need to be made for children and obstetric patients.

Through the incorporation of this guidance into clinical practice, we hope that patients with adrenal insufficiency (from whatever cause) never suffer an adrenal crisis through lack of administration of parenteral glucocorticoid therapy at the time of surgery.

THE NEXT STEPS

Optimising and ensuring the highest quality of care for patients with adrenal insufficiency is paramount. In parallel with this new guidance, ongoing work is bringing together the Society for Endocrinology, the Royal College of Physicians Safety Committee and the British National Formulary, all co-ordinated through NHS England and NHS Improvement. The aim is to further heighten awareness of adrenal insufficiency and its consequences, and to deliver and distribute a new NHS steroid emergency card. This will replace the somewhat outdated blue steroid card that many patients still carry with them. The launch of the new steroid card is imminent: keep watching Society for Endocrinology communications for updates and details.

JEREMY TOMLINSON

Professor of Metabolic Endocrinology, Medical Sciences Division, University of Oxford

HELEN SIMPSON

Consultant Endocrinologist, Department of Diabetes and Endocrinology, UCLH NHS Foundation Trust, London

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READ NEW GUIDELINES FOR MANAGING ADRENAL INSUFFICIENCY

The Society for Endocrinology, the Association of Anaesthetists and the Royal College of Physicians have published new 'Guidelines for the management of glucocorticoids during the peri-operative period for patients with adrenal insufficiency'.

You can access the guidelines from the *Anaesthesia* website: <https://doi.org/10.1111/anae.14963>.

Endocrine Networks

METABOLIC AND OBESITY UPDATE

WRITTEN BY GAVIN BEWICK AND SHAREEN FORBES



I would like to start by thanking the outgoing conveners of the Society for Endocrinology's Metabolic and Obesity Network, Kevin Murphy and Barbara McGowan, who have done a great job marshalling the Network for the last 4 years.

I am Gavin Bewick, who, along with Shareen Forbes, will take on the role of the Network's new co-Conveners.

I work in the Diabetes Research Group at King's College London, which is part of the Diabetes, Endocrinology and Obesity Institute. I hold a long-standing interest in gut-brain signalling and the pathology of the gut in metabolic disease.

Shareen works at the University of Edinburgh in the Centre for Cardiovascular Science. Her research interests lie in the pathology of type 1 and type 2 diabetes, with a focus on β -cell dysregulation and improving islet transplantation outcomes, in both the pre-clinical and clinical settings.

WE WELCOME YOUR IDEAS

We are both very excited about our new roles and aim to serve the Network to the best of our ability. We would like to grow the Network over the next few years, but this will hinge on increased engagement along multiple avenues, ranging from junior and senior researchers to clinicians and allied health professionals. We recognise that growth will be aided by offering interesting and worthwhile initiatives, providing useful up-to-date information and facilitating collaborations.

To do this effectively, we would like to hear your ideas for the Network in the future. We are open to suggestions from anyone. You can contact us directly by email, through the Society, via SfE Connect or via Twitter. In fact, we would like to add dissemination of Network information via Twitter to our current modes of spreading information, so watch this space.

A PRODUCTIVE SfE BES 2019

It was great to attend the annual Society for Endocrinology BES conference in November. The breadth and quality of the science on offer seem to increase every year. From a Network perspective, the new time slot on the final day at 15.00 was a welcome change from the previous early starts, and contributed to an increase in participant numbers. It was good to see a wide range of participants from all walks of Society life, and discussions extended

Kevin Murphy and Barbara McGowan chairing the Network meeting at SfE BES 2019.



from defining clinical guidelines and clinical trial advice to multiple suggestions for symposia.

In my mind, two key themes emerged. There was considerable interest in having symposia focused on nutrition, where we could invite nutritional experts to provide a touchstone for cross-disciplinary collaboration and describe the nutritional evidence base in clinical management of obesity and diabetes. Secondly, there was a groundswell of interest in using the Network to develop clinical guidelines.

'We recognise that growth will be aided by offering interesting and worthwhile initiatives, providing useful up-to-date information and facilitating collaborations.'

THE POTENTIAL FOR GUIDELINES

For example, Eveleigh Nicholson suggested that the increasing incidence of bariatric surgery is naturally producing more patients experiencing post-surgery complications, for which no management guidelines exist. One of the most common complications is post-surgical hypoglycaemia, and the Network agreed that drawing up guidelines to treat people with this complication had a high priority.

This will take some effort, and we would like to put together a working party who would be responsible for defining these guidelines. As such, we would like to hear from anyone who is interested in being part of this initiative. This type of work could become a key part of the Network's role.

I would also like to explore whether the Network could devise initiatives with the aim of calling out and reducing societal stigma against people with obesity.

OBESITY UPDATE 2020

I enjoyed Obesity Update 2020, held at the Royal College of Physicians in London on 13 February. Programme highlights included the year in review, which touched on exercise, personalised medicine and using commercial providers in the management of obesity. The afternoon symposia focused on non-alcoholic steatohepatitis in type 2 diabetes and its treatment. There was also an interesting poster session. As always, the meeting provided excellent opportunities for networking, education and lively debate. I look forward to the 2021 event.

JOIN THE NETWORK TODAY

Above all, Shareen and I look forward to meeting new Network members, who may be encouraged to participate and help shape the Network going forward. Go to the Members' Area at www.endocrinology.org to join Endocrine Networks.

Please keep the conversation going: find us on SfE Connect at www.endocrinology.org/join-sfe-connect.

GAVIN BEWICK

Reader in Endocrinology and Metabolism, King's College London

SHAREEN FORBES

Professor of Diabetic Medicine, University of Edinburgh

Advance your research: EQUIP YOUR LAB USING SOCIETY FUNDS

The Society for Endocrinology Equipment Grant helps members establish their laboratories by funding the purchase of vital equipment. Equipment Grants of up to £10,000 can be awarded for complete items of equipment, parts of larger items or basic lab supplies.

Could you benefit from this funding to get your own lab going?

Read on to discover how previous awardees have used their Equipment Grants to further their research and careers.

Up to two Equipment Grants are offered per year. The next deadline for applications is **6 May 2020**

Visit www.endocrinology.org/grants-and-awards/grants/equipment-grant for more information and to apply.



GISELA HELFER

Lecturer in Medical Sciences,
University of Bradford

Gisela was awarded an Equipment Grant in 2017. Her research aims to understand the role of the adipokine chemerin in hypothalamic and neuroendocrine function, particularly appetite control, growth and energy balance. She used her grant to buy essential equipment to set up small animal brain surgery, which was unavailable at her institution at that point. The data from her initial studies formed an integral part of a successful application for an Academy of Medical Sciences

Springboard Award Grant, and is included in a BBSRC grant application, currently under review.

“The Equipment Grant provides a fantastic opportunity for early career scientists in their first independent position to receive crucial start-up funds, to set up their first lab. In my case, it allowed me to gain important preliminary data to make bigger (successful) grant applications. Without the Equipment Grant, I would not have been able to get this follow-up funding. *Gisela Helfer*”

ASTRID HAUGE EVANS

Senior Lecturer, University of
Roehampton

Astrid was awarded an Equipment Grant in 2016. Her research centres on islet biology and diabetes. The grant enabled Astrid to buy equipment which was fundamental to setting up pancreatic islet isolation and carrying out specific, cell-based assays. Astrid had just started as a Senior Lecturer and needed support to equip her new lab.

She has just published a study featuring the research that was supported by the funded equipment (*Cellular Physiology & Biochemistry* 2019 **52** 486–502).

“Important parts of the work described in our paper were made possible by the Equipment Grant, so I would like to express my thanks to the Society for all their support of our work. It was, and is, much appreciated. *Astrid Hauge Evans*”



JAMES THORNE

University Academic Fellow,
University of Leeds

James was awarded an Equipment Grant in 2016. His research was focused on the paradox that tumours with similar genetic landscapes can have differing prognoses and responses to therapy. His ultimate aim was to identify novel therapeutic targets and improve the prediction of therapeutic responses of breast cancer patients. He used the grant to buy a key instrument for real-time analyses of cell–cell signalling in tumour cells and assessment of the impact of chemotherapy on cultured cells.

His team's new high-throughput assay for measuring chemotherapy drug efflux from cells in culture was successfully designed using the funded plate reader. His pilot data led to the award of a larger project grant. James' team now includes Giorgia Cioccoloni, a post-doctoral researcher funded by Breast Cancer Action, who is running a clinical trial on the effect of sterols on chemotherapy drug efflux, and Alex Websdale, a PhD student funded by Breast Cancer UK, who is evaluating drug efflux in three-dimensional breast cancer spheroids, with a paper on the further research due for submission soon. The Equipment Grant provided the pilot data to obtain funding for both of them.

“This was a fantastic award, and I appreciate the opportunity to say thank you to the Society for supporting my research and career. *James Thorne*”



Colleagues in James' lab:
(L-R) Chrysa Soteriou, Alex Websdale, Giorgia Cioccoloni, Priscilla (Lia) Lianto, James Thorne, Zhi (Rex) Chong.

Meet your new Society President

PROFESSOR RAJ THAKKER



Professor Rajesh Thakker FRS, May Professor of Medicine at the University of Oxford, started his term as Society President at the November AGM. We spoke to him about his hopes and plans for his tenure as President.

TELL US A LITTLE ABOUT YOUR BACKGROUND AND RESEARCH INTERESTS

I specialise in multiple endocrine neoplasia 1 (MEN1) and neuroendocrine tumours. My current research focuses on two main areas. The first is to identify genes whose mutations are involved in causing endocrine tumours and diseases. The second explores mechanisms of G protein-coupled receptor signalling to identify new therapeutic targets.

I started out as a clinician treating patients with MEN, but found they had questions that I just couldn't answer, so I decided to get into research. MEN is a genetic disorder and, at that time, the genetic defect and the underlying molecular and cellular mechanisms causing MEN1 were unknown. So, I retrained in molecular biology – which hadn't even been invented when I was a student! The inspiration partly came from a lecture I attended called 'Stuck at the cell membrane'. It discussed how we were able to target things to the cell membrane, but had no real understanding of what was happening inside the cell. I thought 'that's absolutely right' and decided that investigating genetics would be the way forward for MEN1.

At the Society I've held a number of roles, including serving on Council and being a Convenor for the Endocrine Neoplasia Syndromes Endocrine Network; I've acted as a reviewer, received awards and given multiple presentations. I am really looking forward to making a difference during my presidency.



WHAT ARE YOUR HOPES AND AIMS FOR YOUR TERM AS PRESIDENT?

I think that our Society has a very broad interest base, with top clinicians, scientists and nurses around the country, leading the way and producing high quality work. Endocrinology concerns a multitude of organs and systems, so a lot of what we do is very relevant to other disciplines, including genetics, oncology, biochemistry, nutrition, immunology and pharmacology. I hope to embrace this interdisciplinary aspect during my term.

For example, plans are already underway to include presentations from distinguished leaders working in related disciplines. I hope we can encourage an environment of collaboration, co-operation and inspiration for our members. This is particularly important for our younger members. Looking outside of their discipline is going to be key in advancing endocrinology. There is a huge focus on multidisciplinary research right now, and the Society should be facilitating these relationships too.

Nurturing the next generation is also of huge importance. Graham Williams introduced the Leadership & Development Awards Programme last year to do just this, and we must continue to support and develop the programme to help keep our discipline alive and ready for future challenges.

'Endocrinology concerns a multitude of organs and systems, so a lot of what we do is very relevant to other disciplines, including genetics, oncology, biochemistry, nutrition, immunology and pharmacology. I hope to embrace this interdisciplinary aspect during my term.'

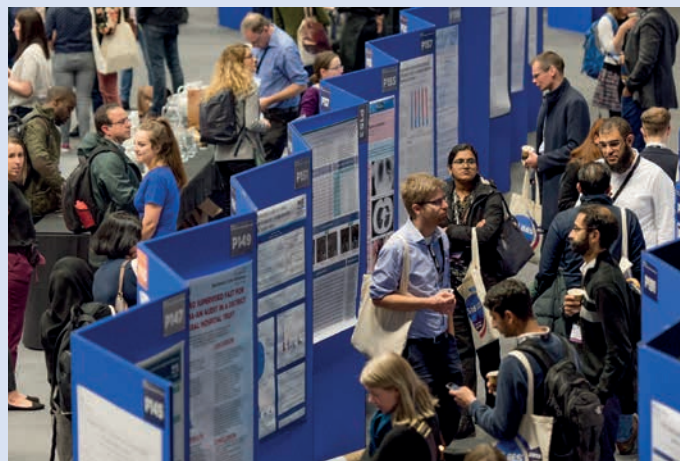


It is also imperative that we provide support for our more established members. We should ensure there are opportunities for clinicians to engage with research. This doesn't just include lab-based work but also clinical trials, public health projects and epidemiological studies. Otherwise, society as a whole is missing out on their talents, as they are unable to engage with research to help improve patient care.

'There is now much more emphasis on multi-disciplinary approaches to science and I believe our plans will be crucial in bringing different segments of our endocrine community together to ultimately help improve patient care.'

Also, we need to attract more research scientists to our annual conference, to facilitate multidisciplinary collaboration, by finding out what they need in order to bring them into our community. If possible, although probably not during my tenure, I'd like to see the Society funding scholarships for researchers. We are a long way from that, but it could make a huge difference to our scientist members and the Society. It could attract some of the top brains to endocrinology to also engage with our clinical members and help improve patient care. I would love to start the ball rolling on something like that. This is obviously expensive, so could be an opportunity to bring our industry partners further into our community, where they could sponsor such scholarships.

I would like to see us strengthening links with our industry partners. We already have some great relationships, but we can make them even more welcome in our endocrine community. This could take the form of more collaborations or sponsorship of various activities. The people working in industry are also top clinicians and scientists, so there are plenty of opportunities for us to work better together, with benefits for both parties.



WHAT ARE THE BIGGEST CHALLENGES FOR THE SOCIETY AND ENDOCRINOLOGY?

A lot of my plans for my term as President aim to tackle some of these challenges.

For example, we are looking at ways to attract research scientists to the Society and our annual conference. One of the biggest challenges in academia right now is the fall in funding and the insecurity of the academic career path. As I mentioned, it would be great if the Society could start some sort of scholarship scheme or find new ways of engaging scientists.

It is also challenging to keep upcoming clinicians engaged with endocrinology as a specialty. I think a lot of our focus is on inspiring the next generation and in supporting talented individuals to become our future leaders.

There is now much more emphasis on multi-disciplinary approaches to science and I believe our plans will be crucial in bringing different segments of our endocrine community together to ultimately help improve patient care.

Some of these ambitions are dreams, but if you don't have them – you'll never achieve them, will you?

TELL US ABOUT YOUR PROUDEST ACHIEVEMENTS

My proudest achievements are the fellows and the students I've trained – they are all now doing fantastic things and I am so proud of them. For example, my first fellow was Dorothy Trump, a registrar in endocrinology. One day, she came to me and told me she thought I'd be disappointed as she'd decided to leave and do genetics. Of course I wasn't, and she went on to become the Chair of Human Genetics at the University of Manchester. Sadly, she passed away about 5 years ago from breast cancer.

Several of my other fellows have also gone on to become more involved with the Society, including Simon Pearce (Newcastle University), Duncan Bassett (Imperial College London), Catherine Williamson (King's College London), Jeremy Turner (Norfolk and Norwich University Hospitals NHS Foundation Trust), Fadil Hannan (University of Oxford) and Paul Newey (University of Dundee), to name just a few. There are so many others.

These students and fellows are my proudest achievements. I'll be really fortunate if anyone remembers an iota of my papers or research in 5–10 years, but the people I've trained will remember me and my legacy will live on through their work. Everyone should take pride in who they train and how this can lead us to accomplish even more.



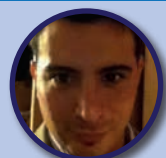
Nurturing ENDOCRINOLOGY'S FUTURE LEADERS

Are you ready to be a future leader in endocrinology?

Applications for the Society's Leadership & Development Awards Programme 2020 open on **1 April** and close on **13 May 2020**.

The Leadership & Development Awards Programme is an ambitious initiative which launched last year to recognise and nurture emerging talent in endocrinology. It forms part of the Society's plan to advance and support our discipline.

Our 12 inaugural Awardees from 2019 are already benefitting from a wide range of opportunities aimed at helping to develop their careers and professional profiles. Could you benefit in 2020?



ALI ABBARA
London



CAROLINE GORVIN
Birmingham



ANNA MITCHELL
Newcastle upon Tyne



RUTH CASEY
Cambridge



**SHAZIA
HUSSAIN**
London



**CATHERINE
NAPIER**
Newcastle
upon Tyne



MYRIAM CHIMEN
Birmingham



KATE LINES
Oxford



MARK NIXON
Edinburgh



CRAIG DOIG
Nottingham



**ZOI
MICHAILIDOU**
Edinburgh



**VICTORIA
SALEM**
London



I feel strongly that the new Leadership & Development Awards Programme will serve the future of the Society and the future of endocrinology well. It will provide unique opportunities for those who apply and I hope it will help to support the careers of our talented trainees.

GRAHAM WILLIAMS
Society President 2016-2019


Benefits available over the course of the 3-year award include:

- expenses-paid attendance at the annual Society for Endocrinology BES conference
- a leadership training course
- a Visiting Fellowship to visit another institution to forge new collaborations or learn new skills
- access to members of an advisory group for *ad hoc* career support and advice
- complimentary membership of the Society for Endocrinology
- experience of the work of the Society's committees, journal editorial boards, working groups, guideline and position statement writing groups and interdepartmental peer review
- opportunities to develop public engagement skills and contribute to public engagement activities.

The Awards Programme aims to identify endocrinology's outstanding early career talent from both clinical and research backgrounds, to prepare the leaders of tomorrow. If you are interested in developing your leadership skills and helping to advance endocrinology, apply for this exciting opportunity and join our 2019 awardees.

Applications are open for the Leadership & Development Awards Programme from **1 April** until **13 May 2020**.

Visit www.endocrinology.org/leadership for more details and full eligibility criteria.



INSPIRE YOUR STUDENTS

Inspire life science students to engage with endocrinology

The Society for Endocrinology is committed to helping you engage your students with hormones. Our Achievement and Video Awards for undergraduates have been created to incentivise and encourage them to really get inside endocrinology, with opportunities to enhance their CVs.



FIND MORE DETAILS AND APPLY AT
endocrinology.org/teach



UNDERGRADUATE VIDEO AWARD

DEADLINE:
30 April 2020

Bringing Endocrinology to Life

Enable your students to delve into the science behind the stories about hormones in the media and communicate them with creativity.

PRIZES:
1st £300
2nd £200
3rd £100



UNDERGRADUATE ACHIEVEMENT AWARD

DEADLINE:
31 July 2020

£300 for teachers to recognise outstanding work from their undergraduate students.



TEACHING ACHIEVEMENT AWARD

DEADLINE FOR
NOMINATIONS:
31 July 2020

Nominate yourself or your colleagues for some well-deserved recognition.

CORTISOL ALERT DOG: IMPROVING PATIENT OUTCOMES?

WRITTEN BY HELEN LOO

Often hailed as a human's best friend, dogs have been the topic of many scientific studies looking into how they might boost our well-being.

I am fortunate to work within a highly specialised team where current evidence is applied to practice and where we aspire to an innovative clinical approach. The phenomenon of medical alert assistance dogs came to my attention while I was caring for a patient with actual/imminent multiple adrenal crises. This experience formed the basis of a poster which I presented at the recent Society for Endocrinology BES conference,¹ where I was delighted to be awarded the Annette Louise Seal Memorial Award from the Addison's Disease Self-Help Group.

WHAT IS A MEDICAL ALERT ASSISTANCE DOG?

The charity Medical Detection Dogs² defines what a medical alert assistance dog does and how it works, as follows.

'Our dogs are trained to alert someone to an impending episode, and allow the person to take preventative medication or safety measures, to either prevent the episode or limit its effects. In order for a dog to alert a person, we must be confident that a chemical process has happened and triggered an odour change in the person that the dog can detect.

'Whilst we acknowledge that a dog also brings about other health benefits, such as companionship, reduced blood pressure and reduced anxiety, evidence shows that medical alert assistance dogs reduce severity of episodes, as well as reducing injuries and visits to hospital.

'They are not trained as emotional support dogs, to provide companionship, friendship and emotional comfort for mental health conditions and, therefore, will not be placed with people who have a predominantly psychological illness.

'Our medical alert assistance dogs are accredited by ADUK (Assistance Dogs UK), working under the umbrella of Assistance Dogs International. Any dog that carries the ADUK badge on its jacket has been shown to meet international standards for obedience and public access requirements, as well as accuracy and reliability for its specific role. These qualities are

Helen receiving the Annette Louise Seal Memorial Award from the Addison's Disease Self-Help Group at SFE BES 2019, alongside (far left) Dr Helen Turner (Consultant Endocrinologist, Oxford Centre for Diabetes, Endocrinology and Metabolism). ©H Loo



assessed every year to ensure that the dog and its handler (your patient) continue to meet these high standards.

'Dogs have an amazing sense of smell, with over 300 million olfactory cells compared to just 5 million cells in humans. We know that changes in the health status of humans can lead to a change in odour, and dogs, with their exceptional sense of smell, are able to detect these minute changes. Evidence now shows that dogs can detect traces of particular types of cancer, low blood glucose levels and types of bacteria from a range of samples, by detecting the distinct change in odour.'

THE CORTISOL ALERT DOG IN DISEASE SUPPORT

In Addison's disease, patient-self maintenance of adequate cortisol levels is essential. Optimising cortisol control is challenging and well documented. Traditional management aims to ensure adequate daily cortisol levels, including stressful situations/acute illness, while avoiding over-replacement.

As mentioned above, dogs are currently used to support patients with hypoglycaemia unawareness. Recent, reported, international studies of equivalent dogs in primary and secondary adrenocorticotropic hormone (ACTH) deficiency are limited. Studies have produced some evidence to suggest that dogs can be trained to detect low cortisol. Further investigation is essential to establish the importance of the use of such dogs.

In the case study we reported at the Society for Endocrinology BES conference 2019, we sought to establish how a medical alert assistance dog could have an impact on optimising ACTH deficiency and improve patient outcomes. We studied one patient and her dog, which was being trained using Pavlovian conditioning to alert the patient to low cortisol levels. To ensure that subjective issues could be discussed, the patient was interviewed using a mixture of open and rating scale questions. The previous results of dynamic testing were compared with those collected during the investigation with the medical alert assistance dog.

The questionnaire showed multiple benefits of having this type of dog. These include enhanced levels of independence, confidence, calmness and well-being. In the patient's words, 'the increased confidence I felt in not missing low cortisol levels made me feel less scared to be on my own and that I'm not taking too much cortisol'.

Preliminary data suggested that a medical alert assistance dog can be successfully trained to detect low cortisol levels. The patient's ability to manage steroid requirements was optimised; her quality of life demonstrated significant improvement.

As an Endocrine Specialist Nurse, this has greatly motivated me, as I have seen the positive impact on patient care and outcomes for this rare, specialist group of patients. I am excited about the future developments and research, which we plan to direct from Oxford, and which the Addison's Disease Self-Help Group and the charity Medical Detection Dogs are keen to support.

HELEN LOO

Department of Endocrinology, Oxford Centre for Diabetes, Endocrinology and Metabolism, Churchill Hospital, Oxford

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ANNE MARLAND

NURSE COMMITTEE CHAIR



Spring is here, bringing with it lots of exciting developments within endocrine nursing.

Our first article of 2020 has been written by Helen Loo from Oxford. Helen informs us of the innovative developments involving cortisol alert dogs and, importantly, how the addition of a dog to the patient clinical care pathway is improving patient outcomes. The charity Medical Detection Dogs helps to explain what a medical alert assistance dog does and how it works. I hope you enjoy the article and are inspired to bring this to your multidisciplinary team discussions. Helen plans to conduct further research with the team in Oxford, and I look forward to the outcomes.

Many of us are very aware of the Addison's Disease Self-Help Group and the amazing work they do. The photo with Helen's article shows her receiving the Annette Louise Seal Memorial Award from them, alongside Consultant Endocrinologist Helen Turner (Oxford), during the Society for Endocrinology BES conference 2019. As an endocrine community we congratulate her and all the team involved.

I hope you have registered for Endocrine Nurse Update in Birmingham on 20–21 April. Our fantastic programme reflects your feedback, and includes our new structure with advance practice sessions and research sessions. You can find it at www.endocrinology.org/events/endocrine-nurse-update/endocrine-nurse-update-2020/scientific-programme.

Do you have a colleague that you would like to nominate for the Society's Endocrine Nurse Award 2021? I encourage you to do so: see www.endocrinology.org/grants-and-awards/prizes-and-awards/endocrine-nurse-award. The closing date is 6 July 2020.

Those of us who were lucky enough to know Nikki Kieffer know that she would have wanted us all to be proud of being an endocrine nurse. I thank Lisa for writing an obituary for Nikki, who will be sadly missed. Our thoughts and sincere condolences go to her husband and family.

Best wishes

ANNE MARLAND

OBITUARY

FEATURE

Remembering NIKKI KIEFFER (1949–2019)



It is with both great sadness and fond memories that I write this tribute to Nikki Kieffer, Endocrine Specialist Nurse at Leicester Royal Infirmary, UK. To those nurses who work or have worked in the specialty, Nikki needs no introduction. Her untimely death in October 2019 has left a void in the world of endocrine nursing.

Nikki was an inspiring and dedicated patient advocate: raising awareness of endocrine conditions amongst healthcare professionals and transforming practice to enhance patient care and outcomes. Her pioneering ways were commended equally by patients and colleagues.

A former Chair of the Society for Endocrinology Nurse Committee and inaugural winner of the Society for Endocrinology Endocrine Nurse Award, she was also a great activist for nurses.

She believed that nurses should advance both academically and professionally.

She has left endocrine nursing a great legacy, having led the development of the *Society for Endocrinology Competency Framework for Adult Endocrine Nursing*.¹ The Framework was designed to improve and provide equitable care for all patients with endocrine conditions, whilst also developing nurses who work in the field. Its conception brought together endocrine nurses globally, forming international collaborations to advance endocrine nursing practice.

Our thoughts and sincere condolences go to Nikki's husband and family.

LISA SHEPHERD

(NURSE COMMITTEE CHAIR 2014–2018)

on behalf of the global community of endocrine nurses

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IMPROVING FEMALE INCLUSION: WITH SUPPORT FROM SfE BES

WRITTEN BY VICTORIA SALEM, ELIZABETH AVIS, JORDAN MCDONAGH AND KEVIN MURPHY

Researchers working with the organisers of our annual flagship event, the Society for Endocrinology BES conference, suggest that this microcosm of the academic environment could be a beacon for improving female inclusion.

Endocrinology is frequently described as a female-friendly clinical specialty. Indeed, gender parity has recently been achieved at training (registrar) grades (data from the Royal College of Physicians). Endocrinology is also popular amongst female research scientists, and very close to half the delegates at our national meeting, the annual Society for Endocrinology BES conference, are women.

However, female academics (both clinical and non-clinical) in endocrinology remain a much smaller minority than should be expected for the gender split at the entry point or the perceived culture of the specialty. The field of endocrinology is therefore a particularly pertinent one in which to examine female academic attrition in more detail.

A number of causes have been suggested for the 'leaky pipeline' of female academics along the academic career trajectory or the lack of women in top clinical or decision-making roles. One widely held belief is that the current proportions amongst senior positions reflects past gender ratios, such that the problem will inevitably correct itself over time (given the increasing proportions of female undergraduates). In fact, the expected improvement has not materialised, and it seems that the continued lack of diversity at senior levels propagates a structural or cultural inertia, in which women continue to fail to progress.

THE CONFERENCE AS A MICROCOSM

Academic conferences are a key element of academic career progression, and are also important for clinicians to remain up-to-date and connected to their specialty. In particular, conferences provide opportunities for increasing visibility. Networking with peers can help generate new research ideas and, importantly, help develop recognition as an expert in one's field.

Mirroring the broader academic landscape, numerous studies suggest that women participate less in academic conferences. For example, women are less likely to be invited as a speaker, and also more likely to decline the invitation. They are more likely to give a poster presentation but less likely to give a talk.

We approached the organisers of the Society for Endocrinology BES conference, to allow us to examine female participation at our national event. We made transcripts of all questions that were asked at the 2017 and 2018 conferences (over 400 questions per conference, spread across more than 40 sessions). We noted the gender of the questioner, whether they were an audience member or a Chair at the session (most conference sessions are moderated by two people), and undertook a qualitative analysis of the language used.

SfE BES 2017: THE ANALYSIS

Despite a gender-balanced audience at the conference in 2017, only 21% of all questions asked at the SfE BES 2017 came from women. Strikingly, only 6 out of 20 sessions chaired by male-only moderators involved a woman asking a question and, in 5 of these, only a single question came from a woman (range 7–18 questions per session). In the other session in which women asked questions, almost half of those questions (5/12) came from women; interestingly, this was the only example where the *opening* question came from a woman. Overall, only 6% of questions asked at sessions with male-only chairs were from women.

Conversely, we studied the sessions at the 2017 conference that were chaired by two women. In this group, 45% of the questions asked were from women, with no instances of a session where either women or men were

entirely excluded from asking a question. Removing the questions asked by the female Chairs themselves, a much lower proportion of questions came from women in the audience (15%), but this was still more than double the proportion that occurred in the sessions chaired only by males, suggesting that female audience members feel more empowered to speak up when there is a female Chair.

THE VIEW AT SfE BES 2018

In 2018, we were very grateful to the conference organisers for attempting to alter the gender balance of the Chairs. Thus, the proportion of sessions with male-only moderators fell from 31% to 21% and the proportion with female-only moderators remained the same at 25%.

It should be highlighted that there were not actually more female Chairs in 2018; rather, women were asked to moderate more than one session. In both 2017 and 2018, 49% of all Chairs were female, thus the *visibility* of female Chairs was enhanced.

Remarkably, the proportion of questions coming from women at the 2018 conference rose to 37% (from 21% in 2017). The analysis from the 2018 conference also confirmed a significant effect of question order – if the first question in a session came from a man, only 29.6% of subsequent questions came from a woman. However, if the first questioner was female, this increased to 46.8%.

Increasing the number of female Chairs is a simple and effective way of improving female inclusion at conferences, and we would strongly recommend that all sessions in future have at least one female Chair.

A QUESTION OF STYLE

The qualitative analysis of the questions asked at the conference, blinded to the gender of the questioner, revealed that men were significantly more likely to ask questions deemed to be aggressive or formulated to display their own knowledge or expertise in a field, as assessed by the blinded observers. Conversely, women were more likely to ask questions that displayed more empathy (for example mentioning specific patients or cases) and, interestingly, to ask more questions about the sexual dimorphic implications of research findings.

One would hope that, with time, increased female visibility will fuel and empower more questions from female audience members. Just as importantly, we would urge all our colleagues to moderate the tone of their questioning style, bearing in mind that more aggressive posturing may dissuade certain groups, more than others, from making themselves heard. If national conferences mirror the broader academic culture, then perhaps we can begin to reflect back a more inclusive image and send a better message to the next generation.

We will be publishing the full results and conclusions of this interventional study shortly. To our knowledge, it is the first of its kind at a national medical conference. We would very much like to extend our gratitude to the organisers of the Society for Endocrinology BES conferences for their help in facilitating this work.

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ANNE WHITE: INTERNATIONAL WOMEN'S DAY INTERVIEW



Anne White is Professor of Endocrine Sciences at the University of Manchester. She leads a research group investigating the interaction between stress hormones and metabolic disease. She is especially well known for the development of assays for measuring adrenocorticotrophin (ACTH) and its precursor pro-opiomelanocortin (POMC). Anne has also held numerous leadership roles, particularly in the field of graduate education.

We're grateful that she gave up some of her time to speak candidly to *The Endocrinologist* about her career as a woman in endocrinology.

THANK YOU FOR AGREEING TO BE INTERVIEWED! CAN WE START BY ASKING YOUR TOP ADVICE FOR AN EARLY CAREER RESEARCHER, BASED ON YOUR OWN EXPERIENCES?

I guess it would be to think very carefully about the research area you are working in. As an early career researcher, following positive results leads you down a certain road which becomes harder and harder to change. You have to be sure it's a route you want to take, and you should consider how receptive you might be to changing course. Otherwise, you may make it hard for yourself when writing grant applications and when trying to take an independent path from your supervisor.

The early stages of my career took me down a technological route, making monoclonal antibodies (MAbs) to small molecules when the technology was new. This turned out to be really challenging, particularly when it came to making MAbs to peptide hormones, because you needed very high affinity and specificity to get MAbs that could be used in diagnostic assays. I made 45 MAbs to ACTH in order to get the characteristics we needed!

The career structure for scientists pursuing technologies was not (and still is not) well established, particularly when I was working as a non-clinical scientist in the clinical setting. I saw clinical endocrinologists forging ahead in their careers, off the back of novel assays that I had introduced. The first author was usually the clinical scientist who collected the patient data, but the novelty came from the assays we were developing.

I decided that the only way forward was take the technologies I had developed and use them to answer scientific questions of my own, using cell culture models to explore ectopic ACTH production by small cell lung cancer cells. Through efforts to get some teaching experience under my belt (by split-site working at the same time as having my first baby!), I was eventually able to secure a lectureship post.

WHAT PERSONAL QUALITIES HAVE INFLUENCED YOUR CAREER PATH?

I wouldn't say that I have a fantastic memory, but I am incredibly well organised. I think this has contributed greatly to my career, simply because it enables me to get things done. I've seen brilliant minds struggle to do good science because they haven't been organised. I also work well as a team player and have had great collaborators, which has certainly contributed to research successes.

I've had quite a few setbacks, which have made me tougher. Without going into details, circumstances in my post-doc period meant that a colleague and I ended up, with little supervision, more or less running the research in the department. That undoubtedly made me stronger.

It takes quite a lot to get me rattled these days, although if someone attacked my research group that would get to me. I am extremely protective of them! I also have very strong values about the quality of experiments and the reasons we work on a particular research area. I can be quite determined in addressing issues such as these.

HOW CAN WOMEN BE SUCCESSFUL, RESPECTED LEADERS?

Leadership is something that I have *learned* to do better. Early on, I found it hard to be a leader. It would really annoy me that people hadn't taken me seriously or ignored my contribution. If I'm honest, my first approach is to be very self-effacing, which can mislead people. I want to be friendly, so I am sometimes not assertive enough. Having had several leadership roles and benefited from a number of management courses, I am now able to tell senior colleagues if they need to improve on something. I'm not sure where the bravery comes from!

Women shouldn't have to adopt a macho attitude to be respected, or perceived as strong characters. In general, we shouldn't encourage this sort of behaviour. We should pull people up for bullying and negative attitudes a lot more than we do, and we certainly shouldn't let them get away with it, just because they have become successful academics. We all struggle with insecurity at times, and it is not helped by competitive behaviour. I think science loses out when it is too competitive, as there are researchers with great ideas who just need more support and encouragement.

Nowadays, I try hard to take a rounded approach to leadership and have a value system where everyone's important. I've had some great experiences in leadership roles; when I was Head of Division, I found the strategic planning really rewarding. If you can help academics find roles that they are really good at, and you can put teams together that work for the good of the whole department, then it makes it more successful. I understand financial planning and how to evaluate options. I was Treasurer of the Society for Endocrinology for 5 years, through some very challenging times!

DO WOMEN NEED TO SUPPORT EACH OTHER BETTER?

Absolutely.

WHAT DO YOU THINK ABOUT INITIATIVES TO IMPROVE GENDER EQUALITY IN SCIENCE? FOR EXAMPLE, MOVES TO INCREASE REPRESENTATION OF WOMEN AT CONFERENCES?

I'm not sure. Do we or don't we need help? Certainly, we need to bring gender equality to the forefront of people's minds and raise awareness. We also need to encourage women to speak up and recognise the situations in which gender may influence behaviour. For example, it's been shown recently that female scientists are less likely to blatantly state the importance of their science; this can have implications for publication success and therefore promotion prospects.

Having said that, there are some simple things which really annoy me! Why are there so many deadlines and meetings in December? Women inevitably have greater carer responsibilities, and this can be one of the busiest times of year. Why do conferences start on a Sunday? This necessitates childcare arrangements, and women often end up missing the first parts of meetings. How do we change these things? Small adjustments could make a very big difference.

Interviewed by Louise Hunter, NIHR Clinical Lecturer, Faculty of Biology, Medicine and Health, University of Manchester

If you would like to learn more about Anne's research, visit

www.research.manchester.ac.uk/portal/anne.white.html